CHAPTER 5

Cornea

Introduction

Applied anatomy

The average corneal diameter is 11.5 mm (vertical) and 12 mm (horizontal). The cornea consists of the following layers (Fig. 5.1):

1. **The epithelium** is stratified, squamous and non-keratinized, and comprises:
   - A single layer of basal columnar cells attached by hemi-desmosomes to the underlying basement membrane.
   - Two to three rows of wing cells.
   - Two layers of squamous surface cells.
   - The surface area of the outermost cells is increased by microplicae and microvilli which facilitate the attachment of mucin. After a lifespan of a few days the superficial cells are shed into the tear film. Because of its excellent ability to regenerate, the epithelium does not scar.
   - The epithelial stem cells are principally located at the superior and inferior limbus and are indispensable for the maintenance of healthy corneal epithelium. They also act as a junctional barrier, preventing conjunctival tissue from growing onto the cornea. Dysfunction or deficiency of limbal stem cells may result in chronic epithelial defects, overgrowth of conjunctival epithelium onto the corneal surface and vascularization. Some of these problems may be prevented by limbal cell transplantation.
2. **Bowman layer** is the acellular superficial layer of the stroma which scars when damaged.
3. **The stroma** makes up 90% of corneal thickness. It is principally composed of regularly orientated layers of collagen fibrils whose spacing is maintained by proteoglycan ground substance (chondroitin sulphate and keratan sulphate) with interspersed modified fibroblasts (keratocytes).
4. **Descemet membrane** is composed of a fine latticework of collagen fibrils. It consists of an anterior banded zone which develops in utero and a posterior non-banded zone laid down throughout life by the endothelium.
5. **The endothelium** consists of a single layer of hexagonal cells. It plays a vital role in maintaining corneal deturgescence but cannot regenerate. With age, the number of cells gradually decreases and therefore neighbouring cells enlarge to fill the space.

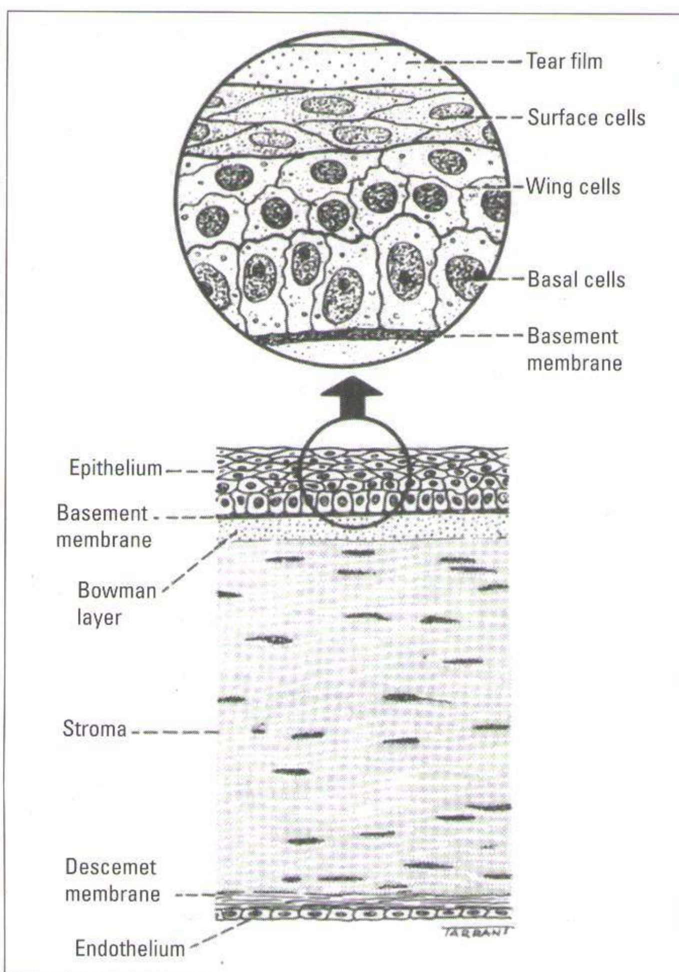


Fig. 5.1
Anatomy of the cornea

> *NB:* The cornea is richly supplied by sensory nerve endings via the first division of the trigeminal nerve. There is a subepithelial and a stromal plexus of nerves. In eyes with corneal abrasions or bullous keratopathy, the direct stimulation of bare nerve endings causes pain, lacrimation and photophobia. Corneal oedema causes diffraction and symptoms of haloes around lights.

Slit-lamp biomicroscopy

It is important to systematically detect clinical signs with regard to position, depth and size by slit-lamp biomicroscopy as follows (Fig. 5.2):

1. **Direct illumination** with diffuse light is used to detect gross abnormalities.
   - A narrow obliquely directed slit-beam to visualize a quadrilateral cross-section of the cornea.
   - Further narrowing of the beam to visualize a very thin optical section.
   - The height of the coaxial beam can be adjusted to measure the size of a lesion.
   - The orientation can be varied by rotating the lamp housing.
   - By passing the beam across the entire cornea, the thickness and depth of corneal lesions can be determined.
   - The nature of the light emitted can be modified by the use of filters. For example, the use of a red-free filter makes red objects appear black, thereby increasing contrast when observing vascular structures or rose bengal staining. A cobalt blue filter is normally used in conjunction with fluorescein.
2. **Scleral scatter** involves decentring the slit beam laterally so that the light is incident on the limbus with the microscope focused centrally. Light is then transmitted

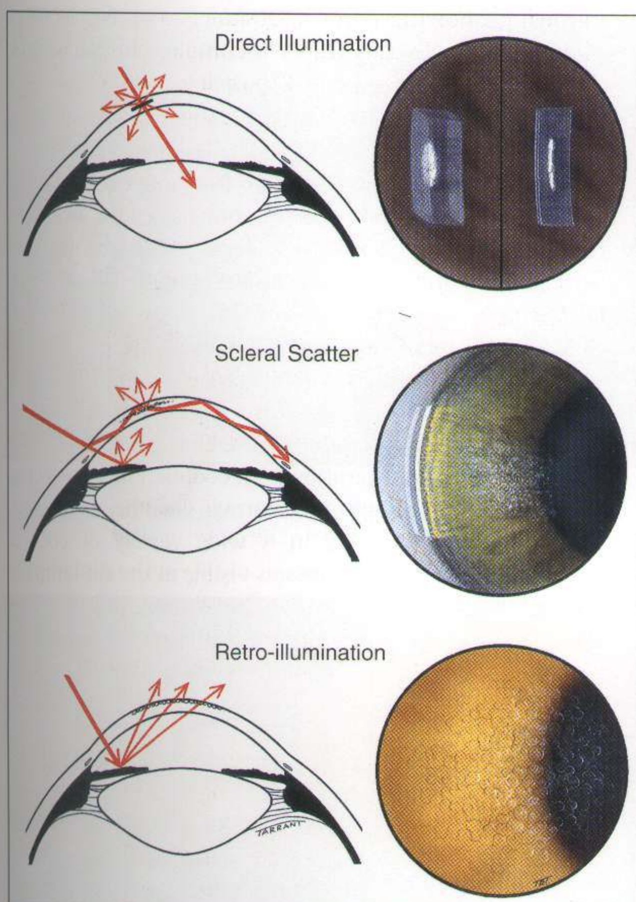


Fig. 5.2
Technique of slit-lamp biomicroscopy

within the cornea by total internal reflection, exiting at the opposite limbus. A corneal lesion will become illuminated because it scatters the internally reflected light beam. This technique is especially useful in the detection of subtle pathology.

3. **Retro-illumination** uses reflected light from the iris or fundus to illuminate the cornea. This allows the detection of fine epithelial and endothelial changes, keratic precipitates and small blood vessels.

Signs of corneal disease

Superficial lesions

1. **Punctate epithelial erosions (PEE)** are tiny, slightly depressed, epithelial defects which stain with fluorescein (Fig. 5.3) but not rose bengal. PEE are non-specific and may develop in a wide variety of keratopathies. Location may frequently indicate aetiology, for example:
   a. Superior. Vernal disease, superior limbic keratoconjunctivitis, floppy eyelids and poorly fitting contact lenses.
   b. Interpalpebral. Dry eyes, diminished corneal sensation and exposure to ultraviolet light.
   c. Inferior. Lower lid margin disease, corneal exposure, rosacea, toxicity from drops and self-induced.

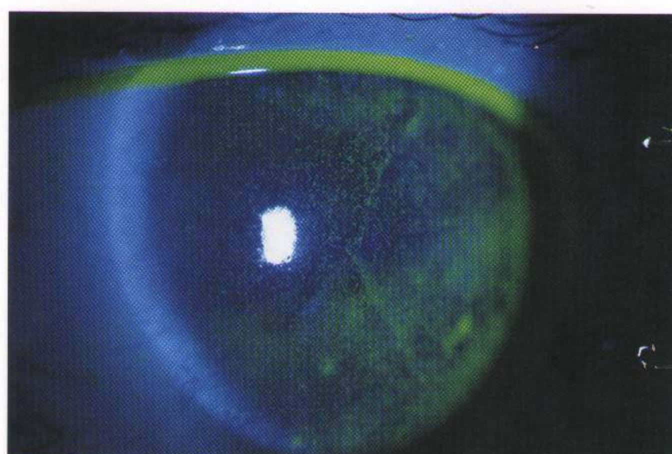

Fig. 5.3
Punctate epithelial erosions stained with fluorescein (Courtesy of A. Bacon)


Fig. 5.4
Punctate epithelial keratitis

2. **Punctate epithelial keratitis (PEK)** is the hallmark of viral infections. It is characterized by granular, opalescent, swollen epithelial cells, visible unstained (Fig. 5.4), which stain well with rose bengal but poorly with fluorescein.
3. **Epithelial oedema** is a sign of endothelial decompensation or severe, acute elevation of intraocular pressure. It is characterized by loss of normal corneal lustre (Fig. 5.5) and, if severe, may be associated with vesicles and bullae (Fig. 5.6).
4. **Filaments**
   a. Signs
   - Small, comma-shaped mucus strands lined with epithelium, attached at one end to the corneal surface (*see* Fig. 3.5); the unattached end moves with each blink. Grey subepithelial opacities may be seen at the site of attachments.
   - They stain well with rose bengal (*see* Fig. 3.5) but not fluorescein, since fluorescein remains extracellular while rose bengal stains dead and degenerating cells and mucus.

   b. Causes. Keratoconjunctivitis sicca, superior limbic keratoconjunctivitis, recurrent erosion syndrome, eye patching,

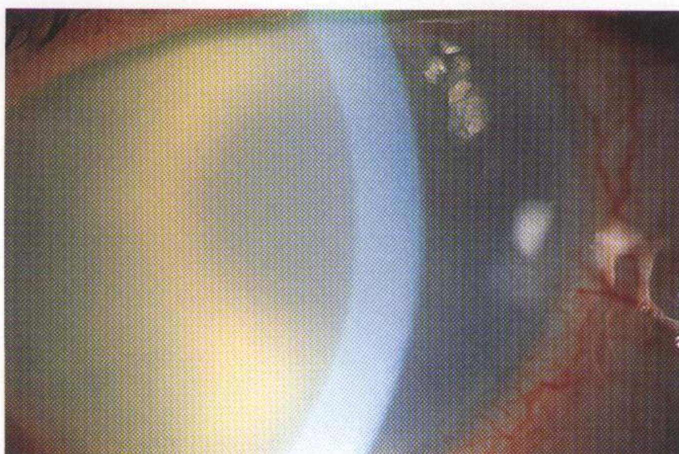

Fig. 5.5
Corneal epithelial oedema


Fig. 5.6
Corneal epithelial vesicles and small bullae

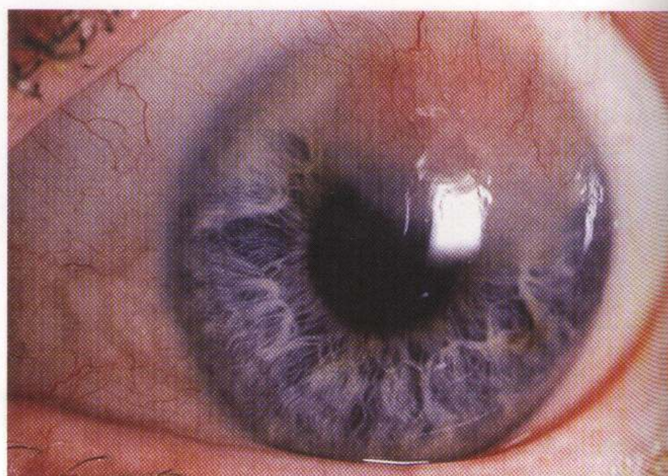
corneal exposure, diminished corneal sensation, herpes zoster ophthalmicus, midbrain strokes and essential blepharospasm.

5. **Pannus** is an inflammatory or degenerative sub-epithelial ingrowth of fibrovascular tissue from the limbus. A progressive pannus is characterized by infiltration extending beyond the ingrowing vessels (Fig. 5.7). In a regressive pannus the vessels extend beyond the infiltrate.

Stromal lesions

1. **Infiltrates** are focal areas of active stromal inflammation composed of accumulations of leucocytes and cellular debris.
   a. Signs
   - Focal, granular, grey-white opacities usually within the anterior stroma and usually associated with limbal or conjunctival hyperaemia (Fig. 5.8).
   - Surrounding halo of less dense infiltration such that individual inflammatory cells may be discernible.

   b. Causes
   - Non-infectious (antigen sensitivity) causes include contact lens wear and marginal keratitis.
   - Infectious keratitis caused by bacteria, viruses, fungi and protozoa. The 'PEDAL' mnemonic is useful in distinguishing non-infectious from infectious infiltrates because the latter are frequently associated with Pain, Epithelial defects, Discharge, Anterior chamber reaction and a more central Location.
2. **Oedema**
   a. Signs. Optically empty spaces between stromal lamellae, associated with increased corneal thickness and variable decrease in transparency as a result of disruption of the regular arrangement (Fig. 5.9).
   b. Causes. Disciform keratitis, keratoconus, Fuchs dystrophy and surgical damage to the corneal endothelium.
3. **Vascularization** occurs in a wide variety of corneal disorders. Corneal blood vessels visible at the slit-lamp are invariably venous (Fig. 5.10). The arterial feeding vessels are difficult to see without fluorescein angiography. Deep vessels are derived from the anterior ciliary vessels and run


Fig. 5.7
Pannus

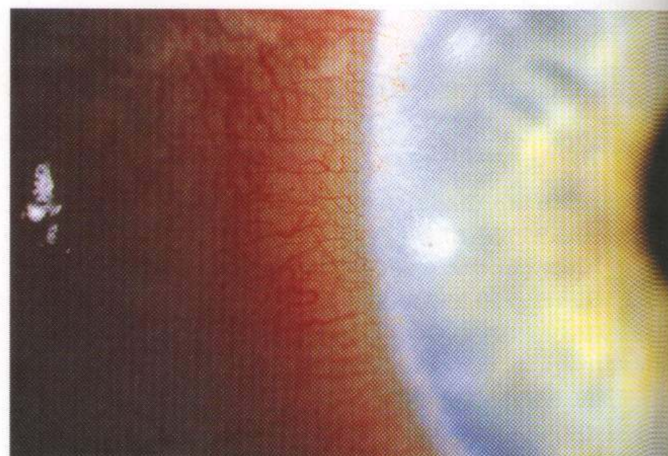

Fig. 5.8
Anterior stromal infiltrates



Fig. 5.9
Stromal corneal oedema

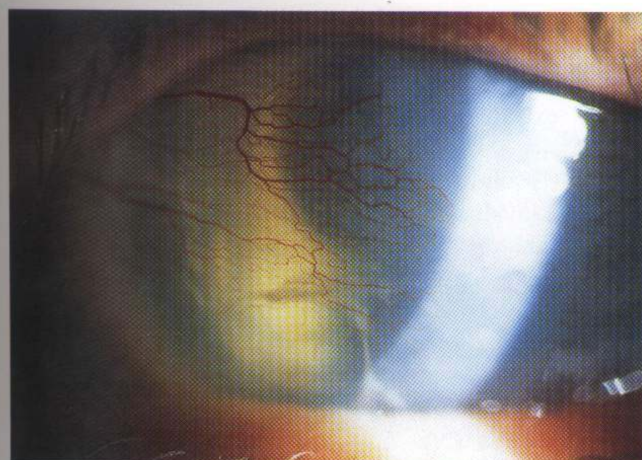


Fig. 5.10
Stromal vascularization

a straight radial course, disappearing at the limbus, unlike wavy superficial vessels which can be traced beyond the limbus. When non-perfused, deep vessels appear as 'ghost vessels', best detected by retroillumination.

Lesions of Descemet membrane

1. **Breaks** (Fig. 5.11) may occur as a result of corneal enlargement, birth trauma and keratoconus and result in acute influx of aqueous into the corneal stroma.
2. **Folds** (striate keratopathy) (Fig. 5.12) may be caused by surgical trauma, ocular hypotony, stromal inflammation and oedema.

Documentation of clinical signs

Frontal and slit views of the cornea are drawn and details added as follows (Fig. 5.13):

1. **Opacities** such as scars and degenerations are drawn in *black*.
2. **Epithelial oedema** is represented by *fine blue circles*, stromal oedema as *blue shading* and folds in Descemet membrane as *wavy blue lines*.
3. **Hypopyon** is shown in *yellow*.



Fig. 5.11
Breaks in Descemet membrane (Courtesy of C. Barry)



Fig. 5.12
Folds in Descemet membrane

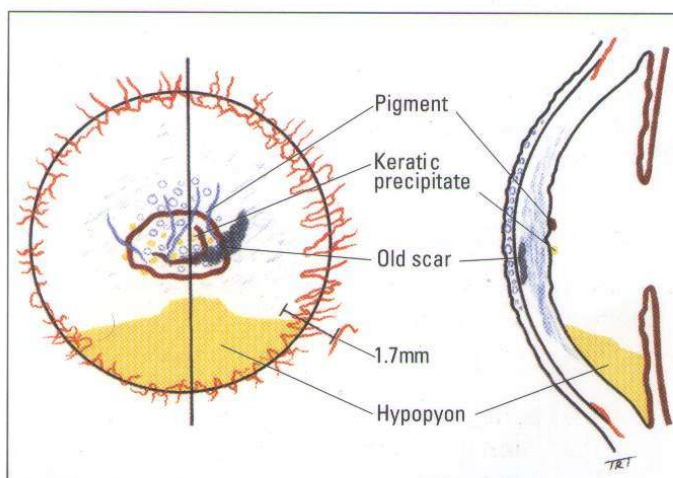


Fig. 5.13
Documentation of corneal lesions

4. **Blood vessels** are then added in *red*. Superficial vessels are wavy lines that begin outside the limbus and deep vessels are straight lines that begin at the limbus.
5. **Pigment** such as iron rings and Krukenberg spindle are shown in *brown*.

Special investigations

Optical methods

1. **Pachymetry** involves measurement of corneal thickness, which is an indirect indication of the integrity of the corneal endothelium. The thickness of the cornea is greatest at the limbus, where it ranges from 0.7 to 0.9 mm. Normal central corneal thickness is 0.49–0.56 mm; readings of 0.6 mm or more are suggestive of endothelial disease.
2. **Specular microscopy** involves photography of the corneal endothelium and subsequent analysis of cellular characteristics such as size, shape, density and distribution (Fig. 5.14). The normal endothelial cell is a regular hexagon. The normal cell density is about 3000 cells per mm^2; counts of below 1000 mm^2 are associated with a significant risk of endothelial decompensation.
3. **Keratometry** involves measurement of the curvature of the axial 2–3 mm of the anterior corneal surface.
   a. Optical principles
   - The cornea acts as a convex mirror with fixed curvatures in each meridian.
   - This allows the positions of two vertical and two horizontal points projected by the instrument to be reflected off the corneal surface. The radius is then measured in millimetres and converted to dioptres.

   b. Limitations
   - The assumption that the cornea is a sphero-cylindrical surface with a single radius of curvature in each meridian, and with major and minor axes at 90° to each other.
   - Keratometry measures only four points approximately 3 mm apart and provides no information about the cornea central or peripheral to the points measured.
   - Mild corneal surface irregularities can cause mire distortion that compromise accuracy. Keratometry is therefore of limited use for measuring corneas that are not sphero-cylindrical, as frequently occurs in refractive surgery, keratoconus and several other corneal abnormalities.
4. **Corneal topography** with computerized videokeratoscopy provides a colour-coded map of the corneal surface. The dioptric powers of the steepest and flattest meridia and their axes are also calculated and displayed.
   a. Indications
   - To quantify irregular astigmatism and corneal warpage associated with contact lens wear.
   - To diagnose early keratoconus. While advanced keratoconus is easy to diagnose, early or subclinical cases pose a diagnostic challenge.
   - To evaluate postoperative changes in corneal shape after refractive surgery, corneal grafting or cataract extraction.

   b. Scales
   - Absolute scales have fixed end-points and each individual colour represents a specific dioptric power interval. Most normal corneas remain within the yellow–green spectrum of the scale (Fig. 5.15). An absolute scale should always be used to facilitate comparison over time and between patients.
   - Relative (normalized) scales are not fixed and vary according to the dioptric range of the individual cornea (Fig. 5.16). It is very important to look carefully at the scale before attempting to interpret the map.

   c. Interpretation can be acquired only by practice. Important questions to be answered are:
   - What scale does the map show?
   - Is the scale appropriate?
   - Is the map reliable?
   - What is the position of the pupil in relation to the curvature pattern display?

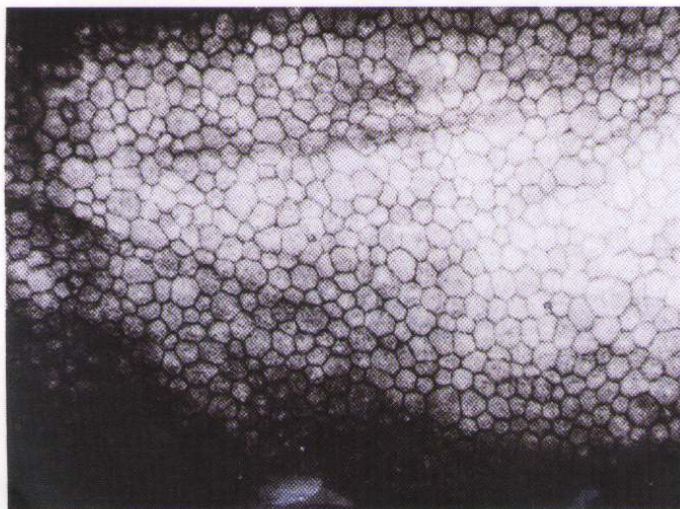


Fig. 5.14
Appearance of normal corneal endothelial cells on specular microscopy

Microbiological investigations

1. **Corneal scrapings** to obtain specimens are made with a Kimura spatula, bent tip of a 21-gauge hypodermic needle or a no. 15 blade. After the instillation of a topical preservative-free anaesthetic, the margins and base of the lesion, usually an ulcer, are gently but firmly scraped under slit-lamp visualization. Contact lens wearers should have their contact lenses and cases sent for microbiological investigation. The material is plated on to glass slides for Gram staining and on to the following culture media as appropriate:
   a. ***Blood agar*** for most bacteria and fungi.
   b. ***Thioglycolate broth*** for most bacteria.
   c. ***Chocolate agar*** for *Neisseria* and *Haemophilus*.
   d. ***Sabouraud agar*** for fungi; this is incubated at room temperature as well as at 37°C.

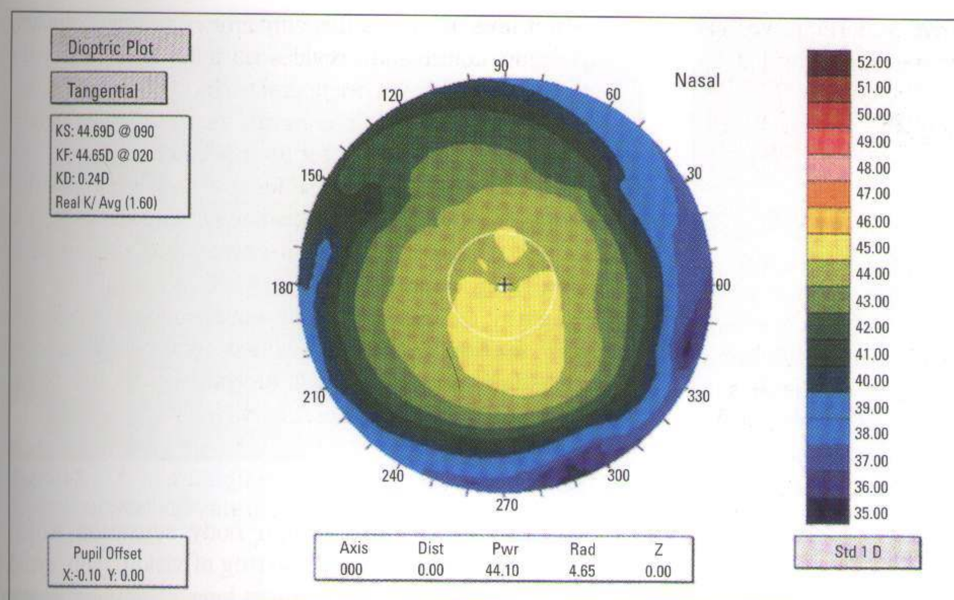


Fig. 5.15
Corneal map showing a normal spherical cornea in an absolute scale ranging from 34 to 54 D with 1 D intervals (Courtesy of E. Morris)

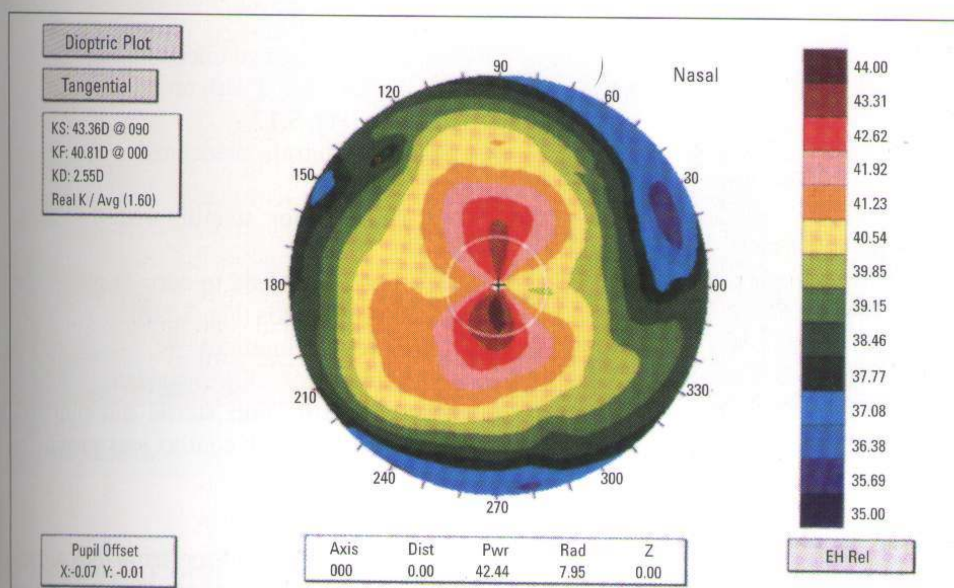


Fig. 5.16
A relative scale of a normal cornea with 3.5 D of with-the-rule astigmatism showing a typical bow-tie pattern (Courtesy of E. Morris)

e. ***Brain–heart infusion broth*** for fungi that fail to grow on Sabouraud agar.

f. ***Non-nutrient agar*** on plates preseeded with an *E. coli* culture for acanthamoeba.

g. ***Buffered charcoal–yeast extract agar*** for acanthamoeba.

NB: Culture media should be at room temperature before inoculation.

2. **Corneal biopsy** can be performed either with a trephine or by free lamellar dissection using a sharp blade. The following are the main indications:
   - Keratitis with negative or non-contributory scrapings and cultures.
   - A corneal infiltrate that is too deep to be reached by simple scraping.
   - To diagnose problematic corneal diseases, such as rare dystrophies or systemic genetic metabolic storage disorders with corneal manifestations.

Principles of management

Control of infection and inflammation

1. **Antimicrobial agents** should be used for corneal infections as soon as preliminary investigations have been completed. Collagen shields may be useful in helping drug delivery. The shield is shaped like a contact lens and is packed in a dehydrated form which requires rehydration before application.
2. **Topical steroids** are used to suppress inflammation and limit scarring, although injudicious use may promote microbial growth. They may also suppress corneal repair, promote ulceration–perforation and are contraindicated in active herpes simplex epithelial disease.
3. **Systemic immunosuppressive agents** may be useful in certain forms of severe peripheral corneal ulceration and melting associated with systemic connective tissue disorders.

Promotion of re-epithelialization

In eyes with a thin stroma it is important to promote re-epithelialization because thinning seldom progresses if the epithelium is intact. The following are the main methods of promoting re-epithelialization:

1. **Lubrication** with artificial tears and ointments, which should not contain potentially toxic (benzalkonium) or sensitizing (thiomersal) preservatives.
2. **Eyelid closure** is particularly useful in exposure and neurotrophic keratopathies as well as in eyes with persistent epithelial defects. It can be achieved by one of the following methods:
   - Taping the lids temporarily with Blenderm or Transpore.
   - Botulinum toxin injection into the levator muscle to induce a temporary ptosis.
   - Lateral tarsorrhaphy or medial canthoplasty.
3. **Bandage soft contact lenses** promote healing by mechanically protecting regenerating corneal epithelium from the constant rubbing of the eyelids.
4. **Amniotic membrane grafting** may be necessary for persistent unresponsive epithelial defects.

Other measures

1. **Tissue adhesive** (cyanoacrylate) glue may be used to limit stromal ulceration and to seal small perforations. It is first applied onto a plastic patch which is then applied to the area of thinning or perforation and a bandage contact lens inserted (*see* Fig. 5.147).
2. **Hooding** with a conjunctival (Gundersen) flap to cover the cornea if ulceration is progressive and unresponsive. This procedure is particularly suitable for chronic unilateral disease in which the prognosis for restoration of useful vision is poor.
3. **Limbal stem cell transplantation** may be required in patients with stem cell deficiency associated with a variety of corneal disorders such as chemical burns or cicatrizing conjunctivitis. The source of the donor tissue may be the fellow eye (autograft) in unilateral disease or from a living or cadaver donor (allograft) when both eyes are affected.
4. **Keratoplasty** may be required to restore corneal transparency.

Microbial keratitis

Bacterial keratitis

Predisposing factors

Bacteria capable of penetrating intact epithelium include *Neisseria gonorrhoeae* and *H. influenzae*. Other bacteria are capable of producing keratitis only after compromisation of epithelial integrity, associated with the following factors:

1. **Contact lens wear**, particularly extended-wear soft lenses, is the most common predisposing factor in patients with previously normal eyes. Meticulous lens hygiene is therefore vital. Epithelial defects commonly occur in contact lens wearers facilitating bacterial colonization, often by *Pseudomonas aeruginosa*. The diagnosis of bacterial keratitis must therefore be considered in any contact lens user with an acutely painful red eye and a white spot on the cornea.
2. **Pre-existing corneal disease** such as trauma, bullous keratopathy, exposure and diminished corneal sensation.
3. **Other factors** include chronic blepharoconjunctivitis, chronic dacryocystitis, tear film deficiency, topical steroid therapy and hypovitaminosis A.

Clinical features

1. **Presentation** is with foreign body sensation which progresses to photophobia, blurring of vision, pain, eyelid oedema and discharge. In contact lens wearers symptoms may be masked or delayed.
2. **Signs** (in chronological order)
   - Conjunctival and circumcorneal injection.
   - An epithelial defect associated with an infiltrate around the margin and base (Fig. 5.17).
   - Enlargement of the infiltrate associated with stromal oedema (Fig. 5.18).
   - Secondary sterile anterior uveitis with hypopyon (Fig. 5.19)
   - Progressive ulceration may lead to corneal perforation and bacterial endophthalmitis (Fig. 5.20).
3. **Differential diagnosis** includes fungal keratitis, acanthamoeba keratitis, stromal necrotic herpes simplex keratitis, marginal keratitis and sterile inflammatory corneal infiltrates associated with contact lens wear.

Principles of treatment

Initial treatment should be with broad-spectrum topical antibiotics because polymicrobial infections are common and an unproductive Gram stain does not exclude bacterial infection.

1. **Dual therapy** involves a combination of two fortified antibiotics to cover common Gram-positive and Gram-negative pathogens, in the form of an aminoglycoside and a cephalosporin.
2. **Monotherapy** with a fluoroquinolone (i.e. ciprofloxacin 0.3% or ofloxacin 0.3%) is easily available but may be associated with corneal toxicity from preservatives.

> ***NB:*** Both cover the majority of pathogens and bacterial resistance is encountered in only about 5% of cases. Fluoroquinolones are only moderately effective against *Strep. pneumoniae*.

Preparation of fortified antibiotics

A standard parenteral or lyophilized antibiotic preparation is combined with a compatible vehicle such that the antibiotic does not precipitate.

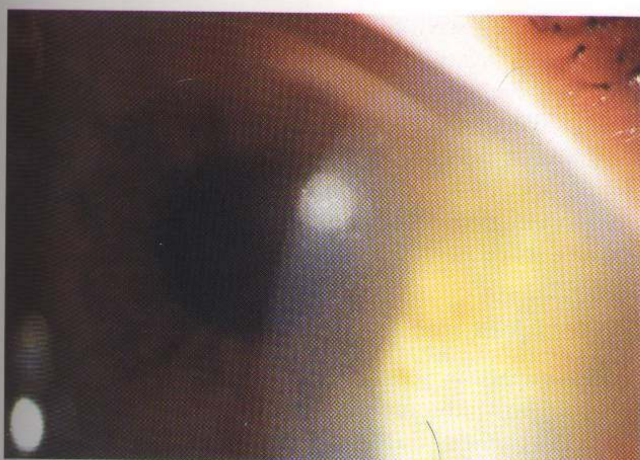


Fig. 5.17
Corneal stromal infiltrate in early bacterial keratitis

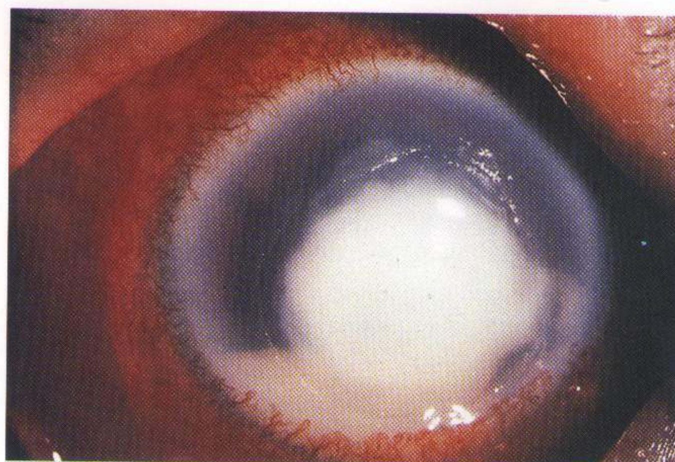


Fig. 5.19
Bacterial keratitis with hypopyon



Fig. 5.18
Bacterial keratitis



Fig. 5.20
Bacterial keratitis with endophthalmitis

1. **Gentamicin** 15 mg/ml (1.5%): 2 ml parenteral antibiotic (40 mg/ml) is added to 5 ml commercially available antibiotic ophthalmic solution (0.3%).
2. **Cephazolin** 50 mg/ml (5%): 500 mg parenteral antibiotic is diluted with 2.5 ml sterile water and added to 7.5 ml of preservative-free artificial tears. This is stable for 24 hours at room temperature or 96 hours if kept in a refrigerator.

> *NB:* Potential problems with fortified antibiotics include cost, limited availability, possibly decreased sterility, short shelf-life and need for refrigeration.

Treatment regimen

1. **Topical antibiotics**
   - Initial instillation is at hourly intervals.
   - If response is favourable, frequency can be reduced to 2-hourly during waking hours.
   - If progress is maintained, fortified drops can be substituted by weaker commercial preparations which are then tapered and eventually discontinued.

> *NB:* It is important not to confuse failure of re-epithelialization, resulting from drug toxicity, with persistent infection.

2. **Oral ciprofloxacin** (750 mg twice daily) may be indicated for a juxtalimbal ulcer to prevent contiguous spread to the sclera. This bactericidal antibiotic is copiously secreted in the tears, and being lipid soluble also has excellent intraocular penetration.
3. **When to change antibiotics?**
   - The initial regimen should be changed only if a resistant pathogen is isolated and ulceration is progressing.
   - There is no need to change initial therapy if this has induced a favourable response, even if cultures show a resistant organism.
4. **Atropine** is used to prevent the formation of posterior synechiae and to reduce pain from ciliary spasm.
5. **Steroid therapy** is controversial.
   - The potential benefits of topical steroids in reducing stromal necrosis and scarring should be weighed

against decreased fibroblast activity and wound healing, which increase the risk of perforation.
- Steroids also have the potential to perpetuate infection and should be used with great caution when pseudomonas has been isolated.
- For these reasons steroid therapy may be initiated only when cultures become sterile and there is clear evidence of improvement, usually 7–10 days after initiation of treatment.

Causes of failure

1. **Wrong diagnosis** caused by inappropriate cultures.
   - The most common causes are unrecognized infection with herpes simplex virus, fungi, acanthamoeba and atypical mycobacteria.
   - The cultures should be repeated on special media such as Lowenstein–Jensen (mycobacteria) and non-nutrient *E. coli* seeded agar (acanthamoeba).
   - If cultures are still negative, it may be necessary to perform corneal biopsy or excisional keratoplasty.
2. **Incorrect treatment** due to inappropriate choice of antibiotics.
3. **Drug toxicity**, particularly by the frequent instillation of aminoglycosides, may cause conjunctival and corneal epithelial changes, and delay healing.

> *NB:* Ciprofloxacin may be associated with white corneal precipitates which may also delay epithelial healing (Fig. 5.21). For this reason, the presence of increasing injection inferiorly associated with irritation despite settling of the corneal ulcer suggests the need to discontinue medication.

Fungal keratitis

Although rare, fungal infection (keratomycosis) may have devastating effects. Fungi can cause severe stromal necrosis and enter the anterior chamber by penetrating an intact Descemet membrane. Once in the anterior chamber, the infection is very difficult to control, in part due to poor penetration of antimycotic agents. The most common pathogens are filamentous fungi (*Aspergillus* and *Fusarium* spp.) and *Candida albicans*. Filamentous keratitis is most prevalent in agricultural areas and is typically preceded by ocular trauma involving organic matter such as wood or plants. Candida keratitis typically develops in association with pre-existing corneal disease or in an immunocompromised patient.

Clinical features

1. **Presentation** is with gradual onset of foreign body sensation, photophobia, blurred vision and discharge. Topical steroids enhance fungal replication and corneal invasion and are often in inappropriate use at the time of diagnosis. Progression is much slower and less painful than in bacterial infection.
2. **Signs** vary with the infectious agent.
   a. ***Filamentous keratitis***
   - A greyish, stromal infiltrate with a 'dry' texture and indistinct margins.
   - Surrounding, satellite, feathery, finger-like lesions and immune ring infiltrates (Fig. 5.22).
   - An underlying endothelial plaque and hypopyon may be present (Fig. 5.23).

   b. ***Candida keratitis*** is characterized by a yellow-white ulcer associated with dense suppuration similar to a bacterial keratitis.

Treatment

Before instituting antimycotic therapy, corneal scraping with a surgical blade should be performed in order to reduce the fungal load and enhance penetration of antifungal agents.

1. **Topical** treatment should be for 6 weeks.
   a. ***Filamentous*** infection is treated with Natamycin 5%. Amphotericin 0.15% may be added as a second agent if necessary.
   b. ***Candida*** infection is treated with imidazole 1% or flucytosine 1%.



Fig. 5.21
Ciprofloxacin corneal precipitates



Fig. 5.22
Filamentous fungal keratitis with small surrounding infiltrates

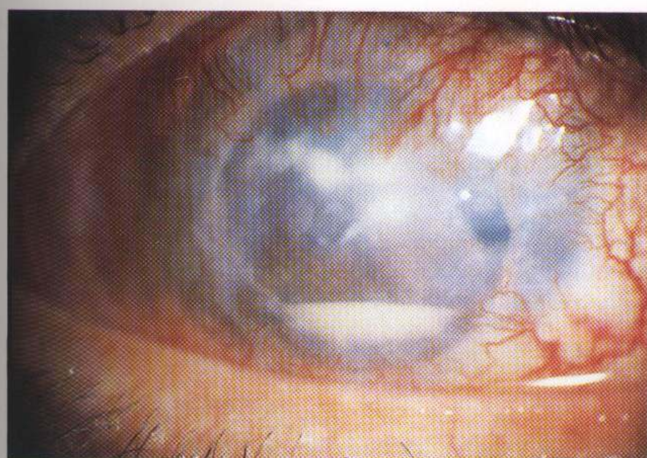


Fig. 5.23
Filamentous fungal keratitis with hypopyon



Fig. 5.24
Anterior stromal infiltrates in acanthamoeba keratitis

2. **Systemic** antimycotics may be required for severe keratitis or endophthalmitis.
3. **Therapeutic penetrating keratoplasty** may be required in unresponsive cases.

Acanthamoeba keratitis

Acanthamoeba sp. are ubiquitous free-living protozoa found in air, soil and fresh or brackish waters. They exist in both active (trophozoite) and dormant (cystic) forms. The cystic form is highly resilient and able to survive for prolonged periods under hostile environmental conditions, including chlorinated swimming pools, hot tubs and subfreezing temperatures in freshwater lakes. Under appropriate environmental conditions, the cysts turn into trophozoites, which produce a variety of enzymes that aid tissue penetration and destruction. Humans are largely resistant, though Acanthamoeba keratitis may occur following a minor corneal abrasion. Contact lens wearers are at particular risk although the infection may be non-contact lens related. *Acanthamoeba* may coexist as an opportunistic organism, particularly in patients with herpetic keratitis.

Clinical features

1. **Presentation** is with blurred vision and severe pain which is characteristically disproportionate to clinical signs.
2. **Signs** (in chronological order)
   - Limbitis, small patchy anterior stromal (Fig. 5.24) and perineural infiltrates (radial keratoneuritis) (Fig. 5.25) are seen during the first 1–4 weeks.
   - The overlying epithelium may be intact or manifest punctate or pseudo-dendritic keratitis (Fig. 5.26).
   - Gradual enlargement and coalescence of the infiltrates may form a central or paracentral ring abscess (Fig. 5.27).
   - Small white satellite lesions may develop peripheral to the ring.

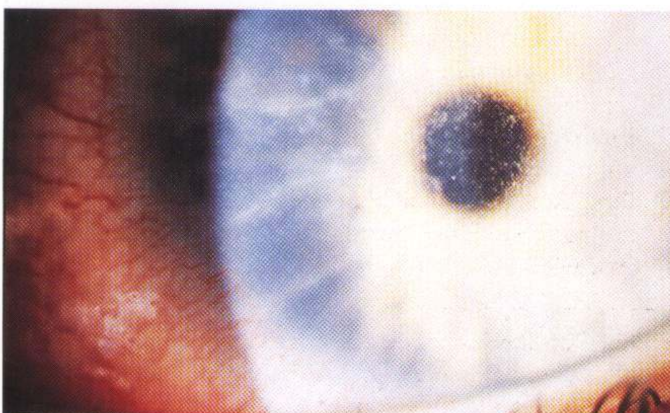


Fig. 5.25
Perineural infiltrates in acanthamoeba keratitis

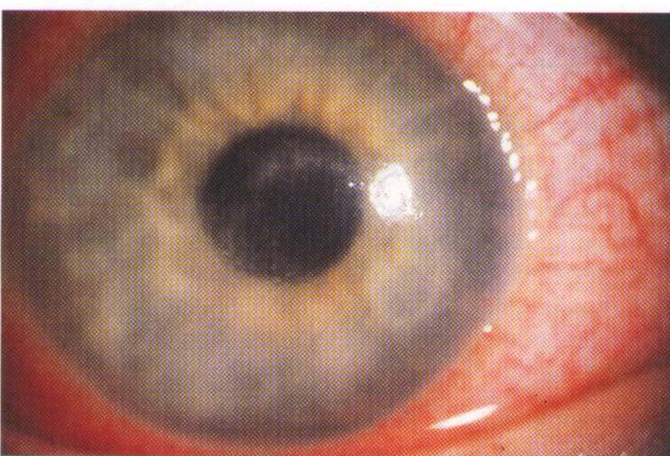


Fig. 5.26
Epithelial changes and pseudo-dendrite in acanthamoeba keratitis (Courtesy of A. Ridgway)

   - Slowly progressive stromal opacification (Fig. 5.28), scleritis and ultimately descemetocele formation.
3. **Differential diagnosis** includes herpetic and fungal keratitis. Important diagnostic clues include soft contact lens wear, severe persistent pain, negative cultures for bacteria,

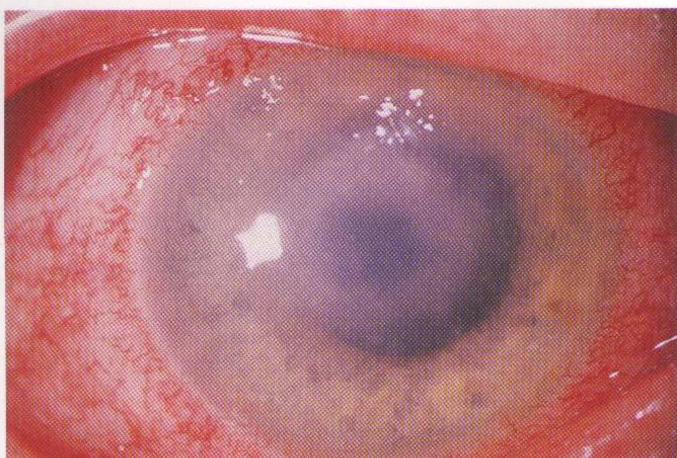


Fig. 5.27
Ring infiltrate in acanthamoeba keratitis (Courtesy of A. Ridgway)

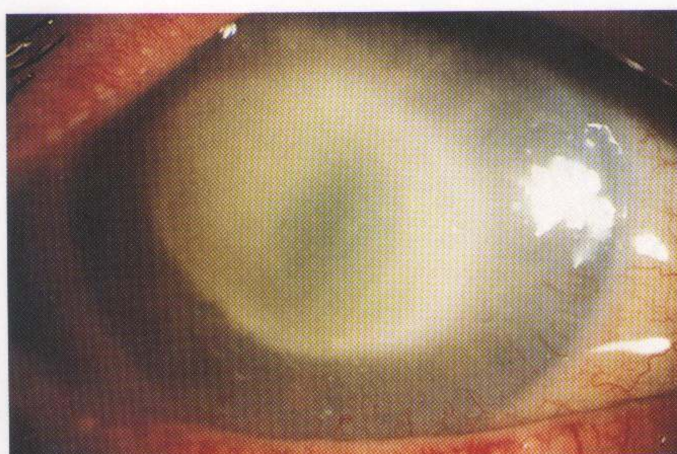


Fig. 5.28
Advanced acanthamoeba keratitis (Courtesy of A. Ridgway)

fungi and viruses and lack of response to conventional antimicrobial therapy.

Investigations

1. **Staining** and microbiological examination of corneal scrapings, biopsy material and contact lenses with calcofluor white, a chemifluorescent dye with an affinity for amoebic cysts.
2. **Cultures** using either non-nutrient agar seeded with *E. coli* or buffered charcoal–yeast extract.

Treatment

1. **Topical amoebicides**
   - A combination of propamidine isethionate 0.1% (Brolene) and polyhexamethylene biguanide 0.02% drops is well tolerated, non-toxic and largely effective.
   - A combination of Brolene and neomycin or monotherapy with chlorhexidine may also give good results.
2. **Topical steroids** may be used to control persistent inflammation but should be terminated before cessation of anti-amoebal therapy.
3. **Therapeutic penetrating keratoplasty** should be avoided in inflamed eyes, but may be necessary in severe cases to preserve the globe or, when the infection has resolved, to restore corneal clarity.

Luetic interstitial keratitis

Interstitial keratitis (IK) is an inflammation of the corneal stroma without primary involvement of the epithelium or endothelium. Apart from congenital syphilis, it may be associated with a wide variety of causes.



Fig. 5.29
Non-perfused 'ghost' vessels in old interstitial keratitis



Fig. 5.30
Intrastromal corneal haemorrhage in old interstitial keratitis



Fig. 5.31
Stromal corneal scarring in old interstitial keratitis

1. **Presentation** is between 5 and 25 years with acute bilateral pain and severe blurring of vision.
2. **Signs** (in chronological order)
   - An inflamed raised sector of limbus from which deep vessels invade the corneal stroma. Associated cellular infiltration and corneal clouding obscure the outline of the vessels, resulting in the characteristic 'salmon-patch'.
   - Anterior uveitis is present but may be obscured by corneal clouding.
   - After several months the cornea begins to clear and the vessels become non-perfused (ghost vessels) (Fig. 5.29).
   - If the cornea later becomes inflamed for any reason, the vessels may refill with blood and, rarely, bleed (Fig. 5.30).
   - Healing is associated with stromal thinning, scarring and often flattening of the cornea.
   - The inactive stage is characterized by a central deep stromal scar of variable density and ghost vessels (Fig. 5.31).
3. **Treatment** of active IK is with systemic penicillin, topical steroids and cycloplegics. Ultimate corneal clarity depends on the extent of vascularization at diagnosis.

Microsporidial keratitis

Microsporidia sp. are small, ubiquitous, obligate intracellular, spore-forming protozoa which are opportunistic pathogens that cause multi-system disease primarily in immunocompromised patients.

1. **Bilateral chronic diffuse punctate epithelial kerato-conjunctivitis** may occur in patients with AIDS. Mild conjunctivitis may occur without keratitis. Treatment is with topical fumagillin and oral albendazole. Highly active antiretroviral therapy (HAART) for AIDS may also be beneficial for the eyes.
2. **Unilateral deep stromal keratitis** affects immuno-competent patients and is very rare. There is no effective treatment and most cases require corneal grafting.

Infectious crystalline keratopathy

Infectious crystalline keratopathy (arborescent bacterial keratopathy) is a rare, indolent infection usually associated with long-term topical steroid therapy, particularly following penetrating keratoplasty. Other risk factors include herpes simplex and acanthamoeba keratitis. *Strep. viridans* is most commonly responsible although other bacteria and fungi have been implicated.

1. **Signs**. Slowly progressive, grey-white, branching opacities in the anterior or mid stroma with minimal inflammation (Figs 5.32, 5.33). Rarely the lesions may involve the epithelium.
2. **Treatment** is with topical antibiotics which have to be used for several weeks.



Fig. 5.32 Early infectious crystalline keratopathy (Courtesy of M. Kerr-Muir)



Fig. 5.33
Advanced infectious crystalline keratopathy (Courtesy of M. Kerr-Muir)

Viral keratitis

Herpes simplex keratitis

Basic concepts

Herpes simplex virus (HSV) is a DNA virus which infects only humans. Infection is common; up to 90% of the population are seropositive for HSV-1 antibodies, although most infections are subclinical. HSV-1 predominantly causes infection above the waist (face, lips and eyes). HSV-2 typically causes venereally acquired infection below the waist (genital herpes). Rarely HSV-2 may be transmitted to the eye through infected genital secretions, either venereally or at birth.

1. **Primary infection** usually occurs in early childhood through droplet transmission, or less frequently by direct inoculation. Due to protection bestowed by maternal antibodies, it is uncommon during the first 6 months of life. Primary infection may be subclinical or may cause mild fever, malaise and upper respiratory infection. In immunocompromised subjects the infection may become generalized and life-threatening.
2. **Recurrent disease**
   - Following primary infection, the virus travels up the axon of a sensory nerve to its ganglion (trigeminal for HSV-1 and spinal for HSV-2), where it lies in a latent state.
   - This latent state may subsequently reverse and the virus reactivates, replicates and travels down the axon of the sensory nerve to its target tissue, causing recurrent disease (genital herpes, herpes labialis and herpetic keratitis).

> *NB:* Without prophylactic treatment (see below) the recurrence rate of herpetic keratitis is about 33% within 1 year and 66% within 2 years.

Primary ocular infection

This typically occurs in children between the ages of 6 months and 5 years, and may be associated with generalized symptoms of a viral illness. Blepharoconjunctivitis is usually benign, self-limited and, in children, may be the only manifestation.

1. **Signs**
   - Skin vesicles typically involve the lids and periorbital area (Fig. 5.34).
   - Acute, unilateral, follicular conjunctivitis associated with preauricular lymphadenopathy.
   - Secondary canalicular obstruction may ensue.
2. **Treatment** is aimed at preventing keratitis with aciclovir eye ointment five times a day for 3 weeks. However, keratitis is uncommon even without antiviral prophylaxis.

Epithelial keratitis

Clinical features

1. **Presentation** may be at any age with mild discomfort, watering and blurring of vision.
2. **Signs** (in chronological order)
   - Opaque epithelial cells arranged in a coarse punctate or stellate pattern (Fig. 5.35).
   - Central desquamation results in a linear-branching (dendritic) ulcer (Fig. 5.36). The ends of the branches manifest a characteristically swollen appearance (terminal bulbs). The bed of the ulcer stains with fluorescein (Fig. 5.37) and the virus-laden cells at the margin of the ulcer with rose bengal (Fig. 5.38).
   - Corneal sensation is reduced.
   - Anterior stromal infiltrates subsequently appear under the ulcer, but usually resolve rapidly once the epithelium has healed.
   - Progressive centrifugal enlargement may result in a larger epithelial defect with a geographical or 'amoeboid' configuration (Fig. 5.39), especially in the context of injudicious topical steroid therapy.
   - Following healing, the epithelium may manifest persistent linear branching shapes which represent waves of healing epithelial cells. These 'pseudodendrites' eventually resolve spontaneously and should not be mistaken for persistent active infection.
3. **Differential diagnosis** of dendritic ulceration includes herpes zoster keratitis, healing corneal abrasion, soft contact lens wear, acanthamoeba keratitis and toxic keratopathies secondary to topical medication (keratitis medicamentosa).



Fig. 5.34
Blepharoconjunctivitis in primary herpes simplex infection

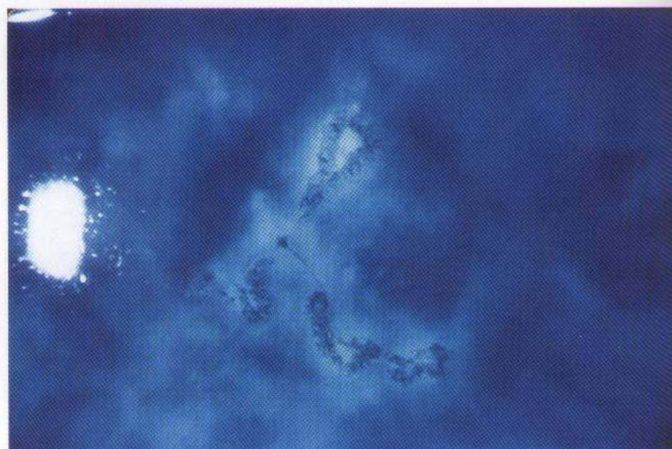
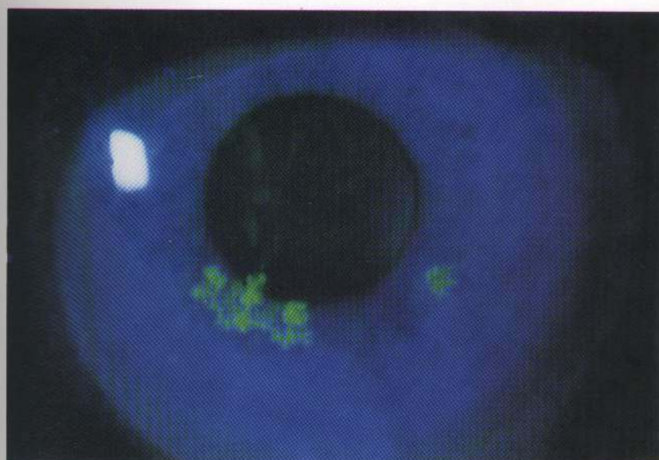
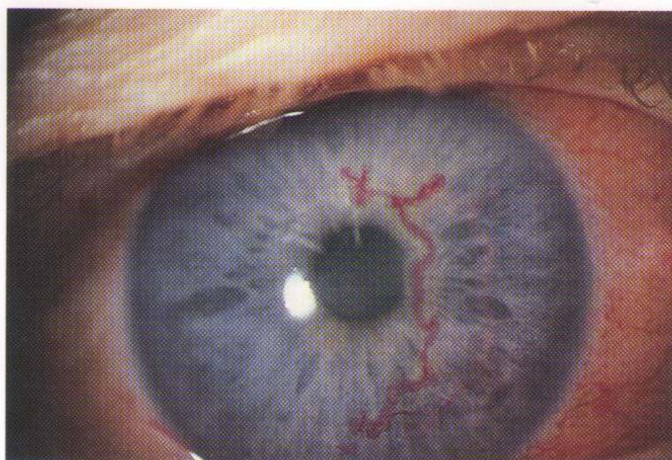
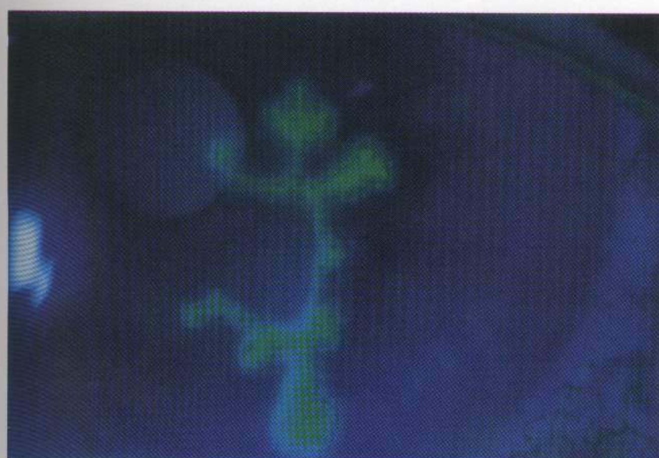
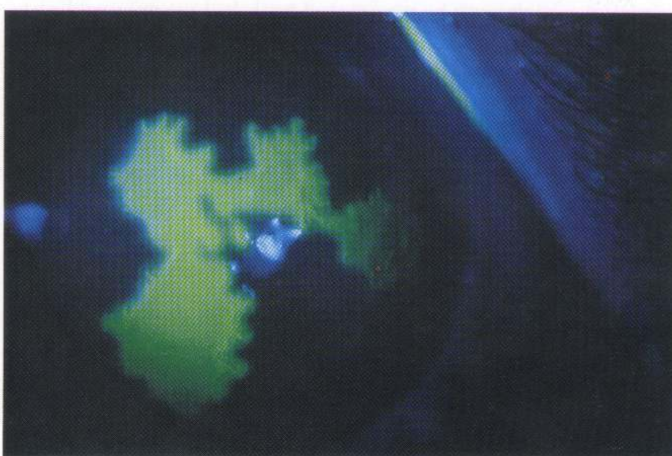


Fig. 5.35
Early dendritic ulcer stained with fluorescein


Fig. 5.36
Small dendritic ulcers stained with fluorescein


Fig. 5.38
Large dendritic ulcer stained with rose bengal


Fig. 5.37
Large dendritic ulcer stained with fluorescein


Fig. 5.39
Geographic ulcer stained with fluorescein

Treatment

1. **Topical**. Even without treatment, about 50% of active epithelial lesions heal spontaneously. The cure rate is in the order of 95% with antiviral therapy. By day 4, the lesion should start to diminish in size, and by day 10 it should have healed. After healing has occurred, medication should be quickly tapered and discontinued by day 14. When treating steroid-enhanced geographic ulcers, the steroid should be withdrawn gradually to avoid rebound worsening.
   a. *Aciclovir* 3% ointment (Zovirax) is used five times daily. The drug is relatively non-toxic, even when given for up to 60 days, because it acts preferentially on virus-laden epithelial cells. It is therefore suitable as antiviral cover to steroids in the management of disciform keratitis, which requires more prolonged treatment than simple dendritic ulceration (*see* below). Aciclovir penetrates intact corneal epithelium and stroma, achieving therapeutic levels in the aqueous humour, and can therefore be used to treat stromal herpetic keratitis.
   b. *Ganciclovir* 0.15% gel (Virgan) is a new preparation which is used five times daily and is as effective as aciclovir.
   c. *Trifluorothymidine* 1% drops (F3T) is used every 2 hours during the day. Like aciclovir, it heals 95% of dendritic ulcers within 2 weeks, exhibits no cross-resistance and has little tendency to produce resistant strains. It is, however, more toxic than aciclovir to the ocular surface epithelium.
2. **Debridement** may be used for dendritic but not geographic ulcers in patients who are non-compliant or allergic to antiviral agents, or if antiviral agents are not available. The corneal surface is wiped with a sterile cellulose sponge 2 mm beyond the edge of the ulcer since pathology extends well beyond the visible dendrite. The removal of the virus-laden cells protects adjacent healthy epithelium from infection and also eliminates the antigenic stimulus to stromal inflammation. Ideally, antiviral agents should be administered following debridement.

Prophylactic systemic therapy

Oral aciclovir 400 mg b.d. for 1 year reduces the rate of recurrent epithelial and stromal keratitis (*see* below) by about 45%

but this effect disappears when the drug is stopped. Prophylactic treatment should be considered mainly for patients suffering two or more attacks of epithelial keratitis annually as well as for those with previous stromal involvement.

Disciform keratitis

The exact aetiology of disciform keratitis (endotheliitis) is controversial. It may be an infection of keratocytes and endothelium or an exaggerated hypersensitivity reaction to viral antigen. A past history of dendritic ulceration is not invariable.

Clinical features

1. **Presentation** is with a gradual onset of painless blurred vision which may be associated with haloes around lights.
2. **Signs**
   - A central zone of epithelial oedema overlying an area of stromal thickening which may be associated with keratic precipitates (Fig. 5.40) and folds in Descemet membrane (Fig. 5.41). Occasionally the lesion is eccentric.
   - A surrounding (Wessely) ring of stromal precipitates may be present, signifying the junction between viral antigen and host antibody (Fig. 5.42).
   - The intraocular pressure may be elevated despite only mild anterior uveitis.
   - Old healed lesions are characterized by a faint ring of stromal opacification that permanently marks the border of the previously oedematous area.
   - Corneal sensation is reduced.

Treatment

Small eccentric lesions may be observed. Large lesions involving the visual axis are treated with topical steroids with antiviral cover as follows:

- Initially the steroid and antiviral are given q.i.d.
- As improvement occurs, the strength of steroid may be reduced and antiviral administered t.i.d. In general, less than 0.25% prednisolone b.d. does not require antiviral cover.
- Steroids should be tapered over a period of several weeks, though one drop a day of a weak concentration for a prolonged period may be necessary to prevent rebound.
- Periodic attempts should be made to taper further or to stop medication altogether.

Stromal necrotic keratitis

Stromal necrotic (infiltrative) keratitis, caused by active viral invasion and tissue necrosis, is rare and may be associated with intact epithelium or may follow epithelial disease.

Clinical features

1. **Presentation** is with progressive impairment of vision associated with discomfort and pain.



Fig. 5.40
Stromal corneal oedema and keratic precipitates in herpetic disciform keratitis



Fig. 5.41
Folds in Descemet membrane in herpetic disciform keratitis



Fig. 5.42
Ring of stromal infiltrates (Wessely ring) in herpetic disciform keratitis

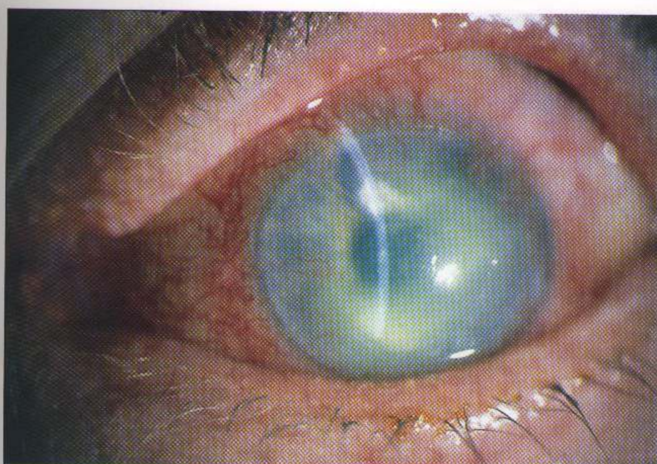


Fig. 5.43
Herpetic stromal necrotic keratitis

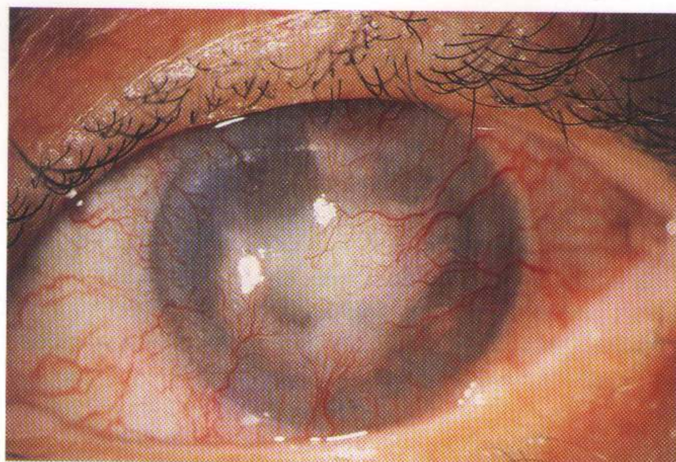


Fig. 5.44
Severe vascularization in herpetic stromal necrotic keratitis

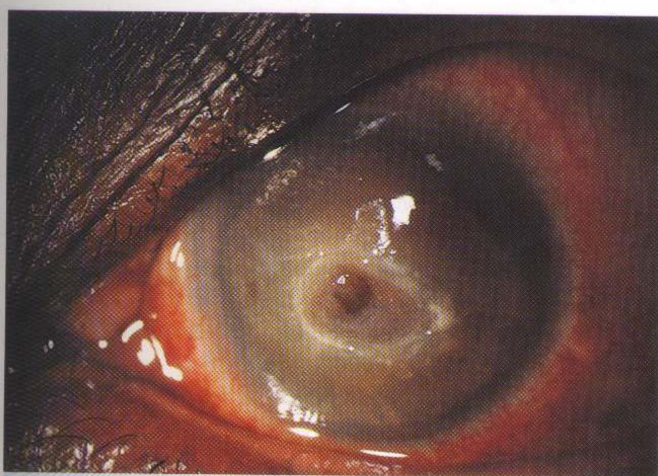


Fig. 5.45
Corneal perforation in herpetic stromal necrotic keratitis

2. Signs

- Cheesy and necrotic stroma reminiscent of a bacterial or fungal infection, or profound interstitial opacification (Fig. 5.43).
- Associated anterior uveitis with keratic precipitates underlying the area of active stromal infiltration.
- If inappropriately treated, scarring, vascularization (Fig. 5.44), lipid keratopathy and even perforation may result (Fig. 5.45).

Treatment

- The first aim is to heal active epithelial disease with antiviral agents.
- Once the epithelium has healed, stromal inflammation may subside. However, in resistant cases with incapacitating symptoms and severe anterior uveitis, the cautious use of steroids, combined with antiviral and antibiotic cover, may be necessary to relieve symptoms and minimize scarring.
- If after 14 days, despite no evidence of active infection, the epithelium is still not healed, treatment is as for neurotrophic keratitis (*see* later).

Herpes zoster ophthalmicus

Herpes zoster (shingles) is a common disease caused by varicella zoster virus (VZV), which is morphologically identical to HSV but different antigenically and clinically. Chickenpox (varicella) and zoster are different conditions caused by the same virus. Zoster mainly affects elderly patients. After an attack of chickenpox, virus remains dormant in sensory root ganglia, perhaps arriving by retrograde spread along sensory nerves from skin lesions. Later, under the influence of largely unknown trigger factors, it reactivates and migrates back down sensory nerves to the skin and eye and causes the characteristic lesions. Virus has been cultured from these sites in the acute stage of the infection.

1. **Ocular damage** may be caused by the following independent or concomitant mechanisms.
   - Direct viral invasion may result in epithelial keratitis and conjunctivitis.
   - Secondary inflammation, occlusive vasculitis and alterations in autoimmune mechanisms may cause stromal keratitis, uveitis, scleritis and episcleritis.
   - Hypoaesthesia may result in neurotrophic keratitis.
2. **Risk of ocular involvement**
   - Approximately 15% of all cases of herpes zoster affect the ophthalmic division of the trigeminal nerve. The condition is then referred to as herpes zoster ophthalmicus (HZO), irrespective of the presence or absence of ocular involvement. Very rarely, the eye may become involved when the disease affects the maxillary nerve.
   - Involvement of the external nasal nerve (Hutchinson sign), which supplies the side of the tip of the nose, correlates significantly with subsequent development of ocular complications because it is the terminal branch of the nasociliary nerve.

- The incidence of HZO increases with age. It occurs most frequently in the sixth and seventh decades.
- In the elderly, the signs and symptoms are more severe and last longer. Patients with AIDS also tend to have more severe disease. There is, however, no correlation between ocular complications and age, sex or severity of the skin rash.

3. Clinical phases

a. Acute, which may totally resolve.
b. Chronic, which may persist for years.
c. Relapsing, where the acute or chronic lesions reappear, sometimes years later.

Acute phase

Systemic features

1. An influenza-like illness with fever, malaise, depression and headache which lasts for up to a week before the appearance of the rash.

2. Preherpetic neuralgia then develops over the distribution of the ophthalmic nerve and varies from a superficial itching, tingling or burning sensation to a severe deep, boring or lancing pain which is either constant or intermittent.

3. Skin rash

- Cutaneous involvement starts with macules which rapidly progress through papules and vesicles to pustules, which begin to crust and scar after a few days (Fig. 5.46).
- The lesions vary in distribution, density and severity and may involve one or more of the cutaneous branches of the ophthalmic nerve. They may be small, discrete and scattered, or large, confluent and deep with haemorrhagic bullae.
- The rash has a dermatomal distribution and respects the midline, although inflammatory oedema may cross the midline, giving the erroneous impression of bilaterality (*see* Fig. 1.20).
- Occasionally the rash may become generalized and the patient severely ill within 1–2 weeks. Such patients often have lymphoma, other malignancies or may be pathologically or iatrogenically immunosuppressed.

Treatment of systemic disease

1. Systemic treatment is with valaciclovir 1 g or famciclovir 250 mg both t.i.d. for 7 days. When administered within 72 hours of the onset of the rash antiviral therapy reduces the incidence of acute ocular complications and also has a beneficial effect on skin lesions.

2. Topical steroid–antibiotic skin creams such as hydrocortisone 1% with fusidic acid 2% (Fucidin-H) or with oxytetracycline 3% (Terra-Cortil) t.i.d. until the crusts have separated.

Keratitis

1. Acute epithelial keratitis develops in about 50% of patients within 2 days of the onset of the rash and resolves spontaneously a few days later. It is characterized by small, fine, dendritic or stellate lesions which stain with fluorescein and rose bengal. In contrast to herpes simplex dendrites, they have tapered ends which lack bulbs (Fig. 5.47).

2. Nummular keratitis may follow, usually about 10 days after the onset of the rash. It is characterized by multiple fine granular subepithelial deposits, surrounded by a halo of stromal haze (Fig. 5.48). They may resolve without trace or become indolent with chronic cellular and lipid infiltration, pannus, scarring, thinning and faceting. The lesions fade in response to topical steroids but recur if treatment is discontinued prematurely.

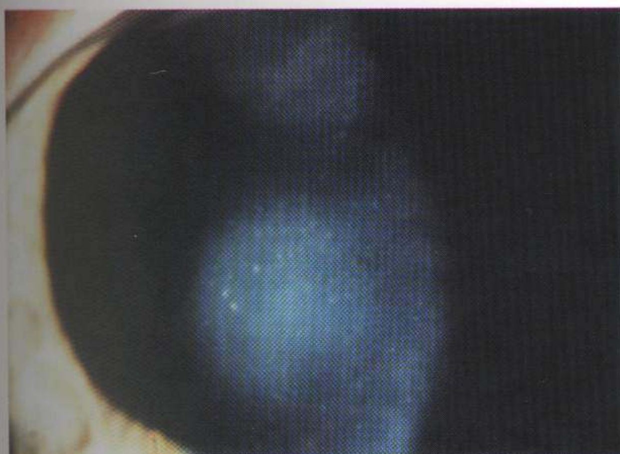
3. Disciform keratitis develops in about 5% of cases, 3 weeks after the onset of the rash. It is usually axial and is almost always preceded by nummular keratitis. If untreated with topical steroids, it almost invariably becomes chronic.



Fig. 5.46
Eyelid involvement in herpes zoster ophthalmicus



Fig. 5.47
Dendritic epithelial lesion in herpes zoster ophthalmicus


Fig. 5.48
Nummular keratitis in herpes zoster ophthalmicus

Other ocular complications

1. **Conjunctivitis** is common and always associated with lid margin vesicles.
2. **Episcleritis**, occurring at the onset of the rash, may be concealed by overlying conjunctivitis and usually resolves spontaneously.
3. **Scleritis** and sclerokeratitis are uncommon and may develop at the end of the first week. If indolent, oral flurbiprofen (Froben) 100 mg t.i.d. may be required.
4. **Anterior uveitis** frequently results in sectoral iris atrophy (*see* Figure 10.49).

Neurological complications

1. **Cranial nerve palsies** affecting the third (most common), fourth and sixth nerves are uncommon and usually recover within 6 months.
2. **Optic neuritis** occurs in about 1:400 cases.
3. **Encephalitis** is rare and only occurs with severe infection.
4. **Contralateral hemiplegia** is also rare, usually mild and typically develops 2 months after the rash.

Chronic phase

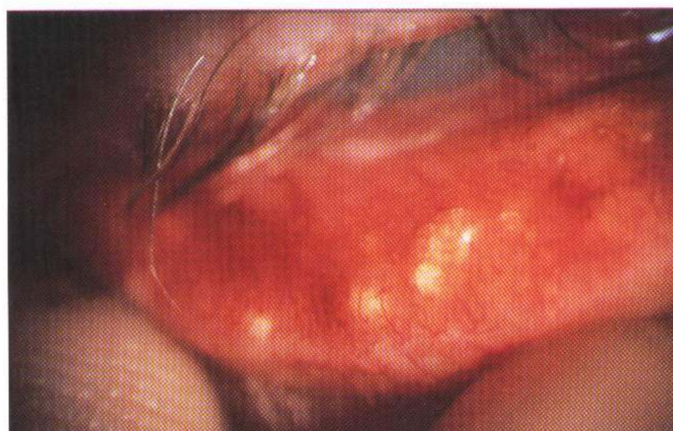
Keratitis

1. **Nummular keratitis** may persist for months, peripheral lesions sometimes forming facets which later become vascularized and infiltrated by lipid.
2. **Disciform keratitis**, if neglected, gives rise to scarring, vascularization and lipid deposition (*see* Fig. 5.83).
3. **Neutrophic keratitis** may lead to severe ulceration, secondary bacterial infection and even perforation.
4. **Mucous plaque keratitis** develops in about 5% of cases, most commonly between the third and sixth months. It is characterized by the sudden appearance of elevated mucous plaques which stain brilliantly with rose bengal (Fig. 5.49). When they assume a dendritiform configuration they may be confused with HSV dendritic ulcers. Treatment involves a combination of topical steroids and acetylcysteine. Untreated, plaques resolve after a few months, leaving a faint diffuse corneal haze.

Other ocular complications

1. **Ptosis** may develop as a result of scarring which may also produce trichiasis, madarosis and notching of the lid margin.
2. **Mucus-secreting conjunctivitis** is a common chronic condition characterized by lipid-filled granulomata under the tarsal conjunctiva and subconjunctival scarring (Fig. 5.50).
3. **Scleritis** may become chronic and lead to patchy scleral atrophy (Fig. 5.51).
4. **Postherpetic neuralgia** may be constant or intermittent, worse at night and aggravated by touch and heat. It generally improves slowly with time, although it may lead to depression, sometimes of sufficient severity to present the danger of suicide. Treatment is with oral amitriptyline and topical capsaicin cream.


Fig. 5.49
Mucus plaques stained with rose bengal in herpes zoster ophthalmicus (Courtesy of R. Marsh)


Fig. 5.50
Lipid-filled granulomata and subconjunctival scarring in herpes zoster ophthalmicus

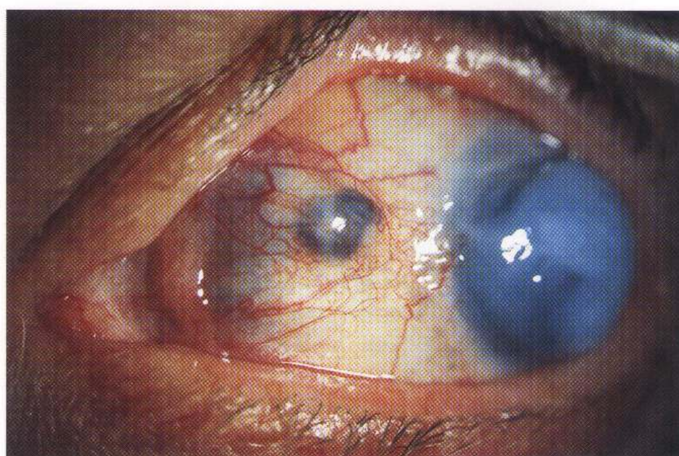


Fig. 5.51
Scleral atrophy and corneal scarring in herpes zoster ophthalmicus

Relapsing phase

Relapsing lesions may reappear even 10 years after acute disease. They may be precipitated by the sudden withdrawal or reduction of topical steroids. The most common lesions include episcleritis, scleritis, iritis, glaucoma and nummular, disciform and mucous plaque keratitis, all of which may appear as isolated lesions because the initial attack of HZO may have been undiagnosed or forgotten.

Thygeson superficial punctate keratitis

Thygeson disease is an uncommon, bilateral, recurrent condition of unknown aetiology. Because a viral cause is suspected it is included in this section.

1. **Presentation** is with ocular irritation and watering.
2. **Signs**. Round or oval conglomerates of distinct, granular, greyish, elevated, punctate epithelial lesions (Fig. 5.52). A mild subepithelial haze may be present, especially if topical antiviral agents have been used.

> *NB:* The conjunctiva is uninvolved.

3. **Treatment** is aimed at relieving symptoms.
   - Lubricants may suffice in mild cases.
   - Topical steroids are effective but may prolong the course of the disease.
   - Bandage contact lenses should be considered in severe cases.



Fig. 5.52
Thygeson superficial punctate keratitis

Peripheral corneal disorders

Dellen

Dellen is caused by localized tear film instability which may be idiopathic or secondary to raised limbal lesions or rigid contact lens wear. It is usually innocuous and transient.

1. **Signs**. Localized, saucer-like thinning of the peripheral cornea, with dehydration of the corneal stroma and compaction of its lamellae (Fig. 5.53).
2. **Treatment** involves eliminating causative pathology and promoting corneal rehydration by padding and topical lubricants.

Marginal keratitis

Marginal keratitis (catarrhal ulcer) is caused by hypersensitivity to staphylococcal exotoxins and is therefore frequently associated with chronic staphylococcal blepharitis (*see* Chapter 1).

1. **Presentation** is in adult life with mild irritation and discomfort.
2. **Signs** (in chronological order)

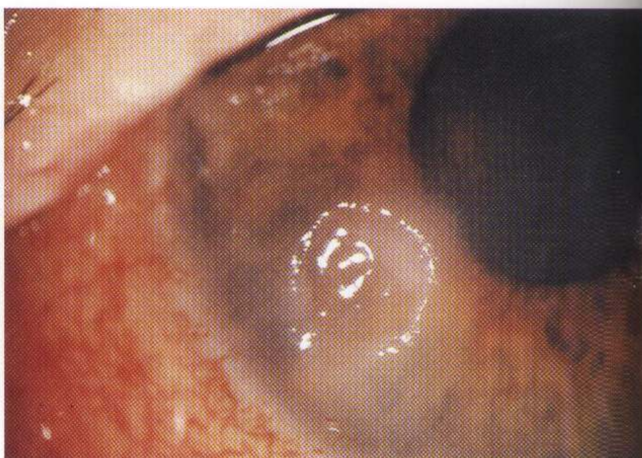


Fig. 5.53
Corneal dellen

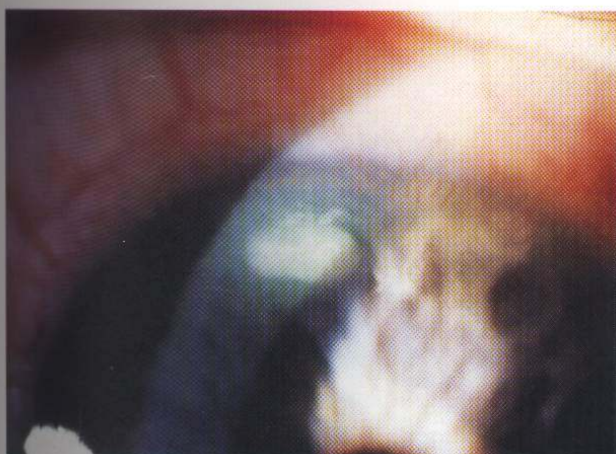
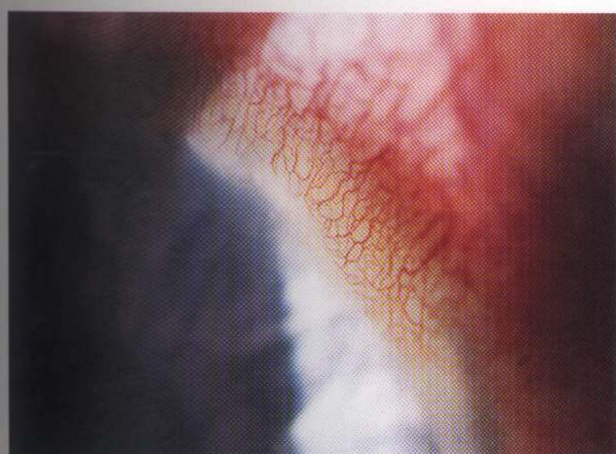

Fig. 5.54
Early marginal keratitis


Fig. 5.55
Severe marginal keratitis stained with fluorescein


Fig. 5.56
Bridging blood vessels in marginal keratitis

- A subepithelial marginal infiltrate separated from the limbus by a clear zone (Fig. 5.54).
- Circumferential spread accompanied by breakdown of the overlying epithelium, giving rise to a fluorescein-staining ulcer (Fig. 5.55).
- Within a few days blood vessels bridge the clear corneal zone and resolution occurs (Fig. 5.56).

3. **Treatment** is with a short course of topical steroids.

> *NB:* Associated staphylococcal blepharitis should also be treated.

Rosacea keratitis

Acne rosacea is a common, chronic, progressive condition of unknown aetiology involving facial skin and the eyes (*see* Chapter 20). The severity of ocular involvement ranges from mild eyelid telangiectasia to corneal perforation. The extent of ocular involvement is unrelated to the severity of cutaneous disease and is often more symptomatic than clinical signs would suggest. Rosacea may therefore be missed if the face is not examined in patients with non-specific ocular symptoms.

Clinical features

1. **Presentation** is with non-specific irritation, burning, tearing and redness.
2. **Signs** (in chronological order)
   - Inferior PEE.
   - Marginal keratitis and peripheral neovascularization, especially involving the inferonasal and inferotemporal cornea (Fig. 5.57).
   - Corneal thinning may occur in severe cases (Fig. 5.58).
   - Perforation may occur as a result of severe peripheral or central melting, which may be precipitated by the excessive use of topical steroids.
3. **Other manifestations**
   a. *Eyelid* involvement includes lid margin telangiectasia, intractable posterior blepharitis and recurrent meibomian cysts.

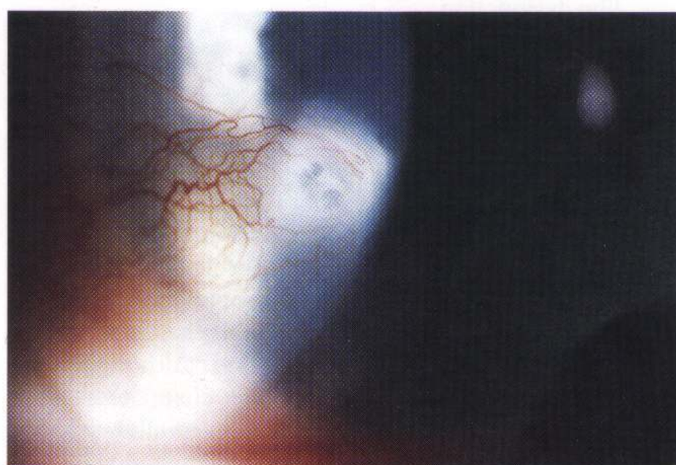
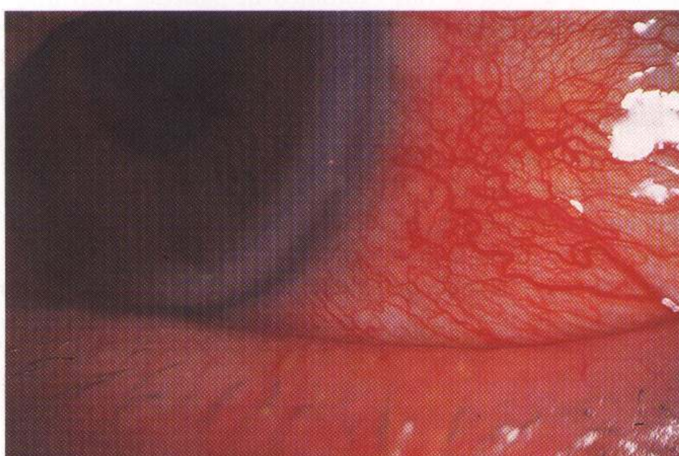

Fig. 5.57
Peripheral corneal vascularization and subepithelial infiltration in rosacea keratitis


Fig. 5.58
Corneal thinning in rosacea keratitis


Fig. 5.59
Conjunctival hyperaemia in acne rosacea

b. ***Conjunctival*** hyperaemia, especially bulbar is common (Fig. 5.59). Other rare findings include cicatricial conjunctivitis, granulomas and phlyctenulosis.

c. ***Miscellaneous*** problems include episcleritis and tear film dysfunction.

Treatment

1. Topical

a. ***Fluorometholone*** as a short-term measure.

b. ***Fusidic acid*** ointment b.d. for 6 weeks.

c. ***Lubricants*** to control tear film dysfunction.

2. Systemic treatment with one of the following antibiotics should be for 6–12 weeks.

a. ***Oxytetracycline*** 500 mg b.d. The therapeutic effect is not related to antibacterial action. Although tetracycline suppresses but does not cure the disease, improvement usually lasts for 6 months after cessation of therapy.

b. ***Doxycycline*** 100 mg once daily is an alternative but, unlike tetracycline, it should be taken in the middle of a meal to prevent gastrointestinal upset.


Fig. 5.60
Yellow dental discoloration and hypoplasia due to systemic tetracycline

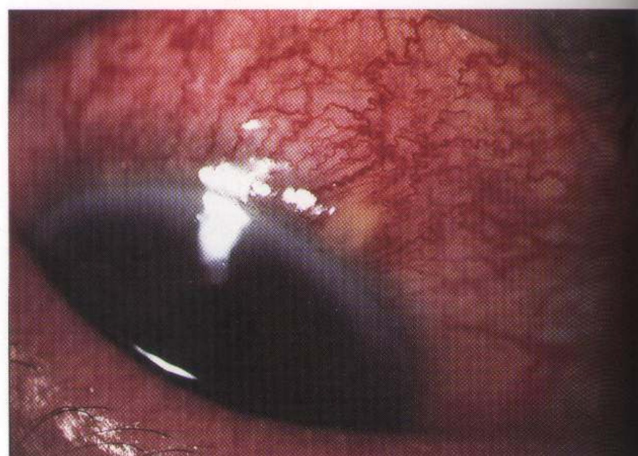
> ***NB:*** Systemic tetracyclines should not be used in children under the age of 12 years or in pregnant or breast-feeding women because the antibiotic is deposited in growing bone and teeth (being bound to calcium), and may cause dental staining and hypoplasia (Fig. 5.60).

c. ***Erythromycin*** 500 mg b.d. if tetracycline is contra-indicated.

Phlyctenulosis

Phlyctenulosis is caused by a non-specific delayed hypersensitivity reaction to bacterial antigens. Although commonly self-limiting the disease may rarely be severe and even blinding.

1. **Presentation** is usually in childhood with photophobia, lacrimation and blepharospasm.
2. **Signs**. A small, pinkish-white, limbal nodule associated with hyperaemia (Fig. 5.61) which may either resolve spontaneously or extend onto the cornea. A healed


Fig. 5.61
Limbal phlycten

corneal phlycten usually leaves a triangular limbal-based scar.

3. **Treatment** is with a short course of topical steroids. Associated chronic staphylococcal blepharitis, which is frequent, should also be treated.

Terrien marginal degeneration

Terrien disease is an uncommon, idiopathic, non-inflammatory thinning of the peripheral cornea. About 75% of affected patients are males and the condition is usually bilateral, although involvement may be asymmetrical.

1. **Presentation** is usually after the fourth decade with initially asymptomatic peripheral corneal lesions.
2. **Signs** (in chronological order)
   - Fine, yellow-white, punctate stromal opacities frequently associated with mild superficial vascularization usually start superiorly, spread circumferentially and are separated from the limbus by a clear zone (Fig. 5.62). On cursory examination they may resemble arcus senilis. This stage is usually asymptomatic and progression is extremely slow.



Fig. 5.62
Early Terrien marginal degeneration



Fig. 5.63
Peripheral corneal thinning in Terrien marginal degeneration

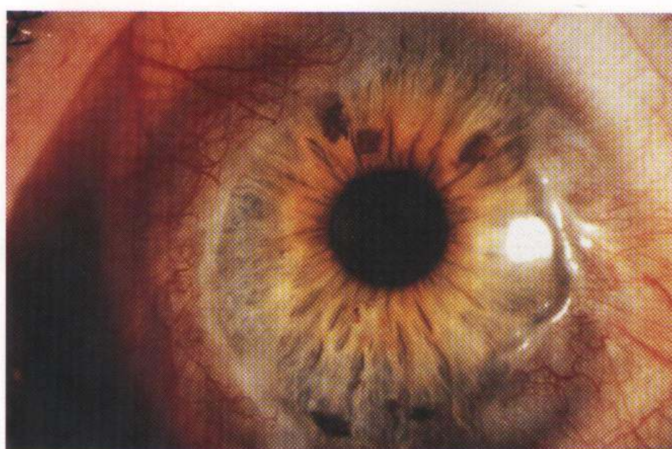


Fig. 5.64
Pseudopterygia in Terrien marginal degeneration

   - Progressive circumferential thinning results in a peripheral gutter, the outer slope of which shelves gradually, while the central part rises sharply (Fig. 5.63).
   - The floor becomes vascularized but the epithelium remains intact.
   - Gradual visual deterioration occurs as a result of increasing corneal astigmatism.
   - A few patients develop recurrent episodes of disabling pain and inflammation.
   - Pseudopterygia may develop in long-standing cases at positions other than the 9 o'clock and 3 o'clock meridia (Fig. 5.64).
3. **Treatment** of significant astigmatism is primarily with gas-permeable scleral contact lenses. While surgery involving crescent-shaped excision of the gutter with suturing of the 'healthier' margins is possible, the results are not ideal and contact lenses are usually necessary to achieve best acuity.

Mooren ulcer

Mooren ulcer is a rare but serious condition probably caused by an autoimmune response to corneal stromal antigens.

Classification

Based on clinical features, fluorescein angiographic findings and response to treatment, the following three distinct types are recognized:

1. **Unilateral ulceration** primarily affects elderly white people, usually female.
   a. *Signs*. Extremely painful, progressive ulceration associated with obliteration of the superficial juxtalimbal vascular plexus.
   b. *Treatment* is difficult as the response to both topical and systemic immunotherapy is poor. The results of corneal grafting are also unsatisfactory, with recurrence of ulceration in the graft.

2. **Bilateral aggressive ulceration** occurs primarily in young males of Indian origin. It is less painful than the unilateral type.
   a. *Signs.* Progressive circumferential ulceration with late centripetal spread. Fluorescein angiography shows neovascularization with leakage extending into the base of the ulcer.
   b. *Treatment* is initially with intravenous methylprednisolone followed by topical and systemic steroids or cytotoxic agents. Topical and systemic cyclosporin may also have a role.
3. **Bilateral indolent ulceration** usually affects middle-aged malnourished patients of Indian origin.
   a. *Signs.* Uncomfortable progressive peripheral guttering with minimal inflammatory response which frequently resolves spontaneously.
   b. *Treatment* involves improving diet and addressing any associated infection.

Signs

Signs (in chronological order), common to all forms of Mooren ulceration are:

- Peripheral corneal infiltration 2–3mm from the limbus (Fig. 5.65).
- Crescent-shaped corneal ulceration characterized by extensive undermining of the leading edge over the infiltrates (Fig. 5.66).

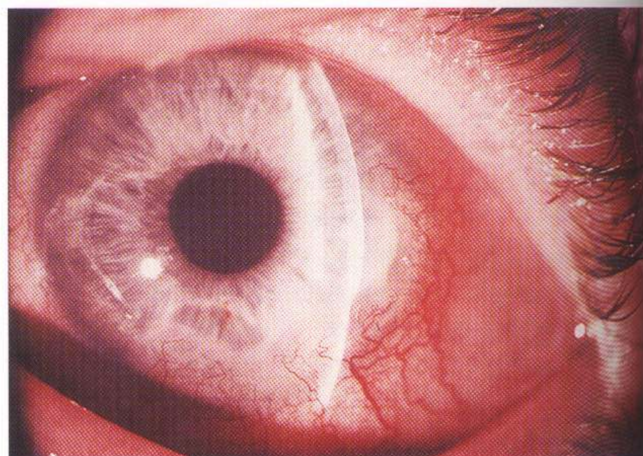


Fig. 5.67
Circumferential spread of Mooren ulcer

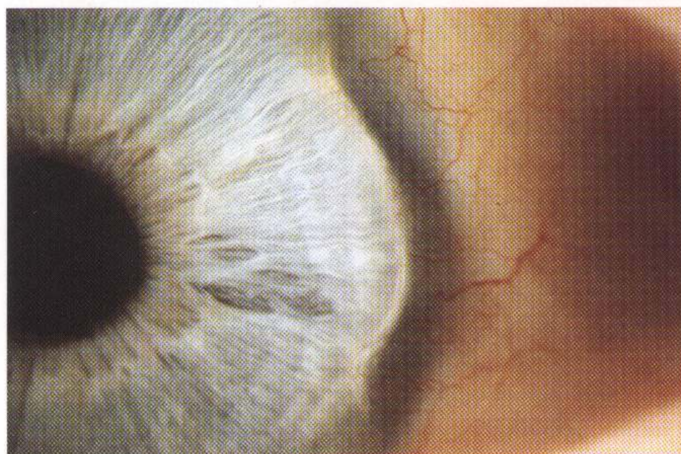


Fig. 5.65
Peripheral corneal infiltration in early Mooren ulcer



Fig. 5.68
Central spread of Mooren ulcer

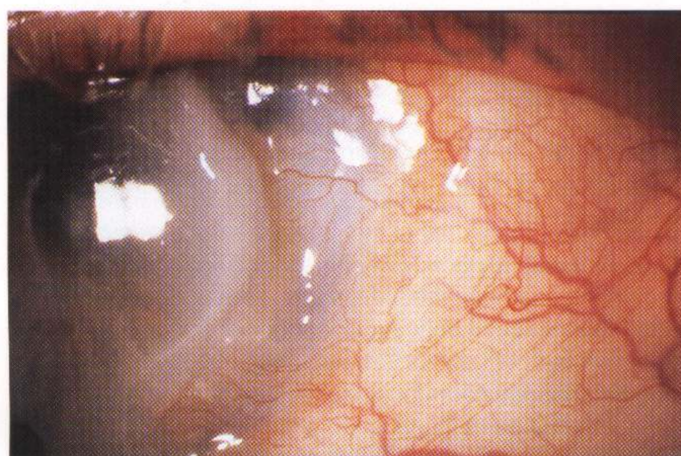


Fig. 5.66
Peripheral ulceration in Mooren ulcer (Courtesy of P. Watson)

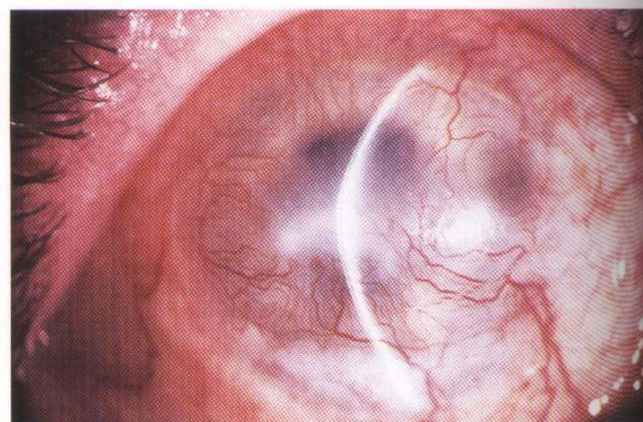


Fig. 5.69
Corneal vascularization and opacification in healed Mooren ulcer

- Circumferential (Fig. 5.67) and central spread (Fig. 5.68).
- The healing stage is characterized by thinning, vascularization and scarring (Fig. 5.69).
- Secondary cataract may form but perforation is rare and the sclera remains uninvolved.

Ulcerative keratitis in systemic disorders

Severe, persistent, peripheral corneal infiltration, ulceration or thinning unexplained by coexistent ocular disease should prompt a search for an associated systemic collagen vascular disorder. The main diseases that should be considered are: (a) *rheumatoid arthritis* and (b) *systemic vasculitides*, such as Wegener granulomatosis and polyarteritis nodosa (*see* Chapter 20). Ocular lesions may precede systemic manifestations.

Keratitis in rheumatoid arthritis

Signs

Keratitis may be primary or secondary to scleritis and may take the following forms:

1. **Sclerosing keratitis** is characterized by gradual thickening and opacification of the corneal stroma adjacent to a site of scleritis (Fig. 5.70). The pathology may extend centrally and be complicated by scarring, vascularization and lipid deposition (Fig. 5.71).
2. **Peripheral corneal thinning** (contact lens cornea) is characterized by gradual resorption of peripheral stroma, leaving the epithelium intact. The normal central cornea resembles a contact lens placed on the eye (Fig. 5.72).
3. **Acute stromal keratitis** is characterized by peripheral infiltrates associated with non-necrotizing scleritis (Fig. 5.73). Late complications include diffuse peripheral scarring and vascularization, and occasionally epithelial breakdown and stromal melting.
4. **Acute corneal melting** may occur in an area of thinned peripheral cornea of the non-inflammatory contact lens type (Fig. 5.74) or, more commonly, in association with intense inflammation at the limbus (Fig. 5.75). The central cornea may also be involved (Fig. 5.76).



Fig. 5.70
Sclerosing keratitis (Courtesy of P. Watson)

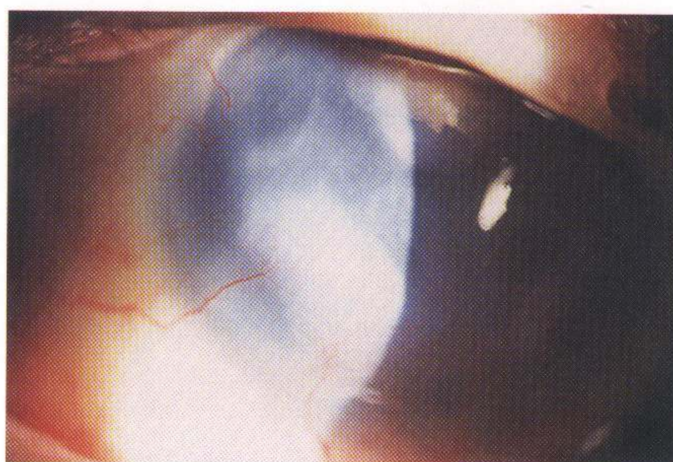


Fig. 5.71
Corneal vascularization and scarring in long-standing sclerosing keratitis

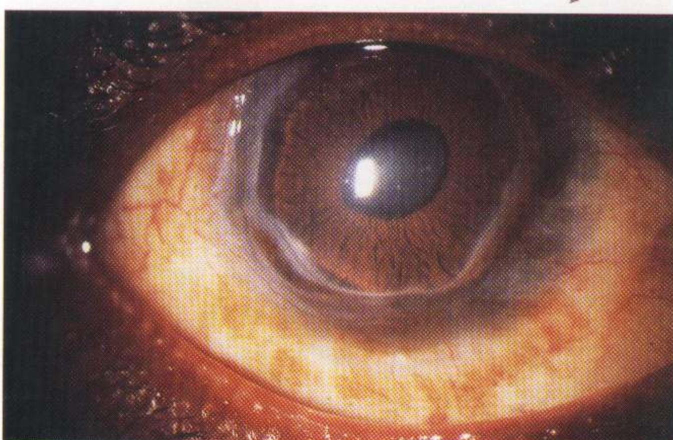


Fig. 5.72
Peripheral corneal thinning without inflammation (contact lens cornea) in rheumatoid arthritis (Courtesy of P. Watson)

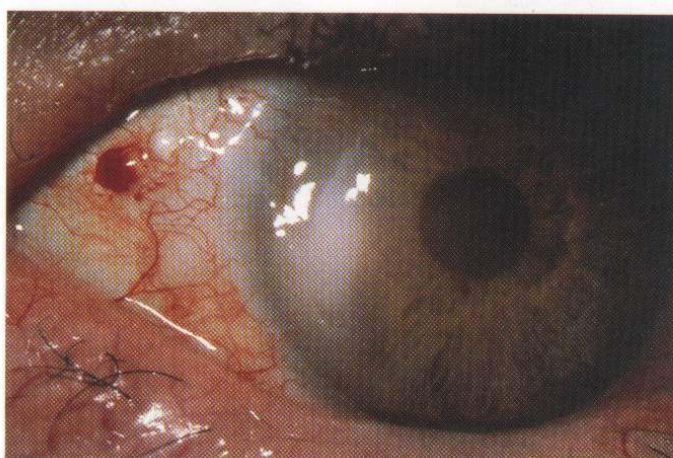


Fig. 5.73
Acute stromal keratitis in rheumatoid arthritis

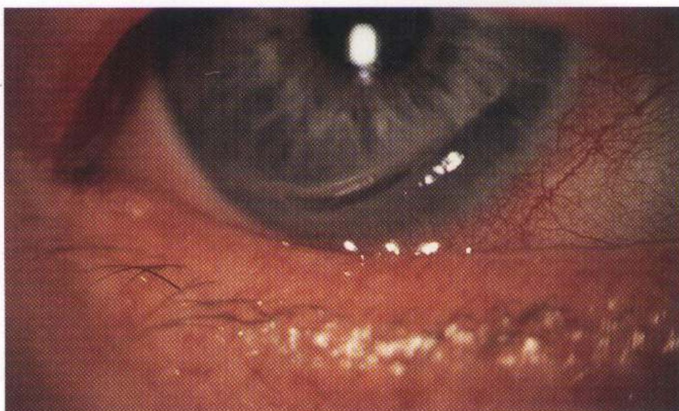


Fig. 5.74
Acute peripheral corneal melting without inflammation in rheumatoid arthritis (Courtesy of P. Watson)

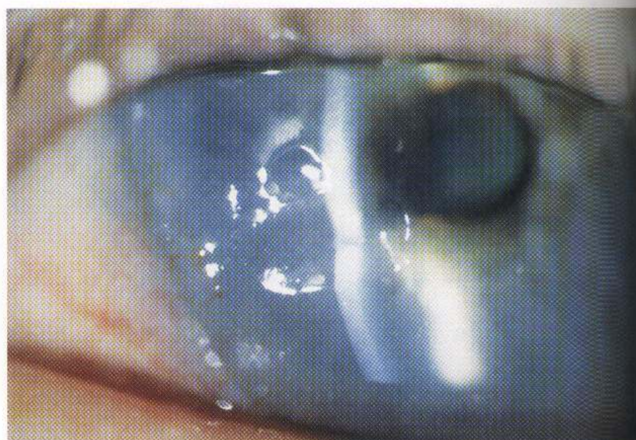


Fig. 5.76
Acute central corneal melting in rheumatoid arthritis

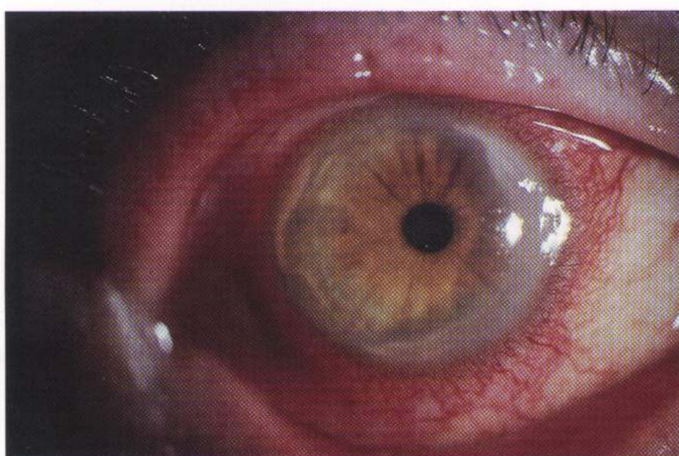


Fig. 5.75
Acute peripheral corneal melting with inflammation in rheumatoid arthritis (Courtesy of P. Watson)

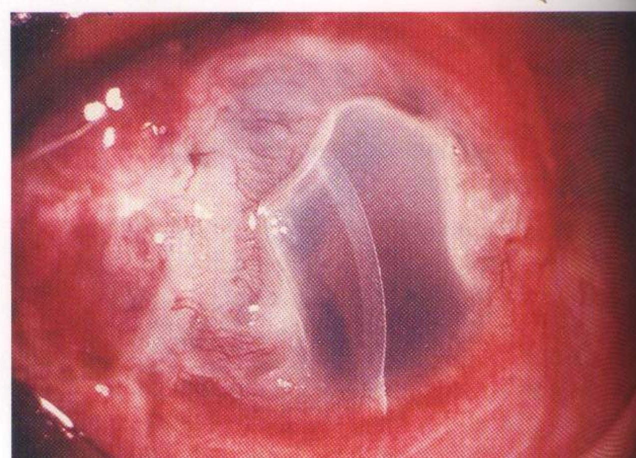


Fig. 5.77
Severe ulcerative keratitis in polyarteritis nodosa

Treatment

1. **Topical**
   a. ***Steroids*** may be useful in acute keratitis but should be avoided in peripheral corneal guttering and keratolysis for fear of potentiating perforation.
   b. ***Cyclosporin*** may also be beneficial.
2. **Systemic** steroids and/or cytotoxic drugs are required for scleritis.
3. **Keratoplasty** may be required either as an emergency measure to prevent perforation, or electively, to restore visual acuity.

Keratitis in systemic vasculitides

1. **Signs** (in chronological order)
   - Bilateral marginal stromal infiltrates.
   - Breakdown of the overlying epithelium.
   - Circumferentially and occasionally central spread similar to a Mooren ulcer (Fig. 5.77).
2. **Treatment** with a combination of systemic steroids and cyclophosphamide may be beneficial.

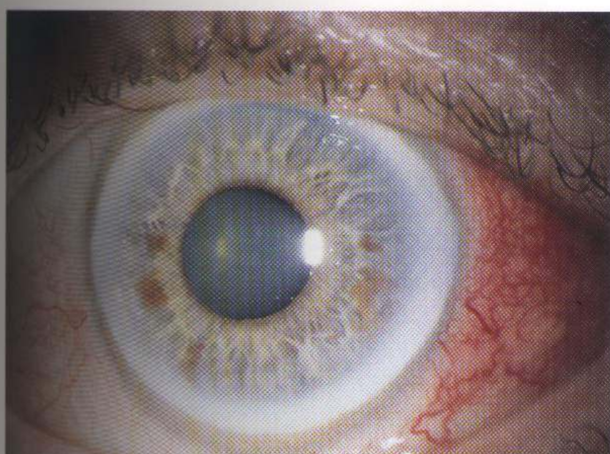
> *NB:* Unlike Mooren ulcer the process may also extend to involve the sclera.

Corneal degenerations

Age-related degenerations

Arcus senilis

1. **Systemic implications**. Arcus senilis is the most common peripheral corneal opacity which frequently occurs without predisposing systemic conditions in elderly individuals. Occasionally arcus may be associated with familial and non-familial dyslipoproteinaemias. Hyperlipoproteinaemia, most notably type II, is frequently associated with bilateral arcus, with less common association in types III, IV and V. Unilateral arcus is a rare entity that may be associated with carotid disease or ocular hypotony.

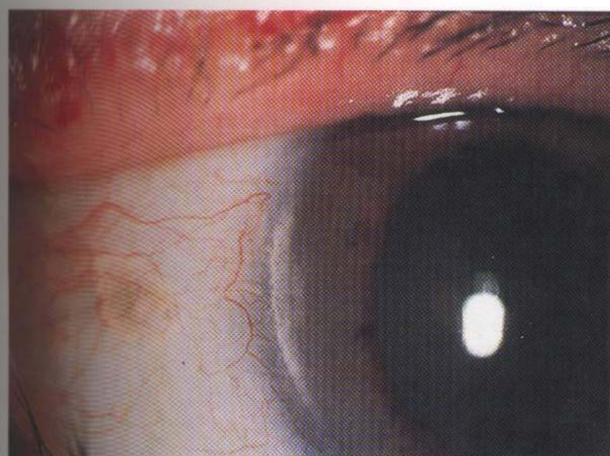

Fig. 5.78
Arcus senilis

Arcus has also been noted in patients with Schnyder crystalline corneal dystrophy.

2. **Signs** (Fig. 5.78)
   - Lipid stromal deposition which starts in the superior and inferior perilimbal cornea and then progresses circumferentially to form a band about 1 mm wide.
   - The band is usually wider in the vertical than horizontal meridian.
   - The central border of the band is diffuse; the peripheral edge is sharp and separated from the limbus by a clear zone.
   - This lucid interval may occasionally undergo mild thinning (senile furrow).

Vogt limbal girdle

This is a common, innocuous, age-related finding characterized by bilateral, narrow, crescentic lines composed of chalk-like flecks running in the interpalpebral fissure along the nasal and temporal limbus (Fig. 5.79). Type 1 is separated from the limbus by a clear interval but type 2 is not.


Fig. 5.79
Vogt white limbal girdle

Cornea farinata

This is a visually insignificant condition characterized by minute, usually bilateral, flour-like deposits in the deep corneal stroma, most prominent centrally (Fig. 5.80).

Crocodile shagreen

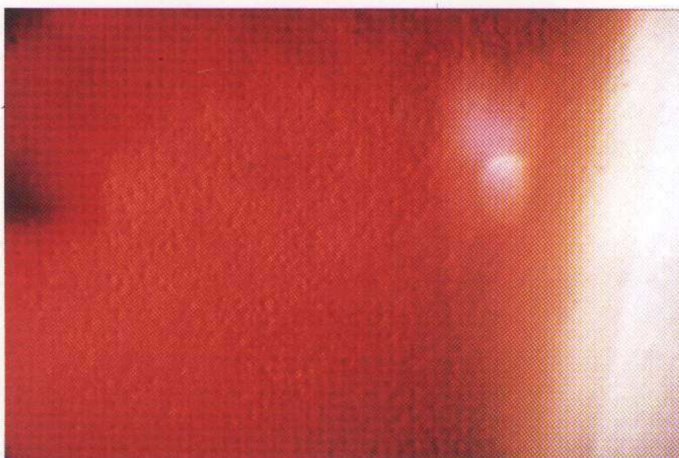
This is characterized by usually asymptomatic, greyish-white, polygonal stromal opacities separated by relatively clear spaces (Fig. 5.81). The opacities most frequently involve the anterior two-thirds of the stroma (anterior crocodile shagreen), although on occasion they may be found more posteriorly (posterior crocodile shagreen).

Cornea guttata

This consists of focal accumulations of collagen on the posterior surface of Descemet membrane. The lesions appear as warts or excrescences and are secreted by abnormal


Fig. 5.80
Cornea farinata


Fig. 5.81
Crocodile shagreen


Fig. 5.82
Cornea guttata

endothelial cells. Examination by specular reflection shows tiny dark spots caused by disruption of the regular endothelial mosaic (Fig. 5.82). In more advanced cases, there is a 'beaten metal' appearance which may be associated with melanin deposition. When the lesions involve the corneal periphery, they are called Hassall–Henle bodies and are of no particular significance except as an indication of ageing. The term 'cornea guttata' is reserved for lesions involving the central cornea, which though usually innocuous, may rarely be indicative of early Fuchs endothelial dystrophy (*see* below). It is therefore important to examine the endothelium carefully prior to cataract surgery.

Lipid keratopathy

1. **Primary** lipid keratopathy is rare and occurs spontaneously. It is characterized by white or yellowish stromal deposits consisting of cholesterol, fats and phospholipids.
2. **Secondary** lipid keratopathy is much more common and is associated with previous ocular injury or disease which has resulted in corneal vascularization (Fig. 5.83). The most common causes are herpes simplex and herpes zoster disciform keratitis. It is associated with corneal vascularization and without treatment is progressive.
3. **Treatment** is primarily aimed at medical control of the underlying inflammatory disease. Other treatment options include the following:
   a. ***Argon laser photocoagulation*** to the arterial 'feeder' vessels may induce resorption of the lipid infiltrate provided they can be identified by fluorescein angiography.
   b. ***Needle point cautery*** may also be successful. It is performed by grasping a 6 mm or similar suture needle in thermal cautery forceps and applying the hot needle tip to the feeder vessels at the limbus under microscopic control.
   c. ***Penetrating keratoplasty*** may be required in advanced but quiescent disease, although vascularization, thinning and hypoaesthesia may prejudice the outcome.

Band keratopathy

Band keratopathy is a common condition characterized by the deposition of calcium salts in the anterior portion of Bowman membrane.

1. **Causes**
   a. ***Ocular*** causes, the most common, include chronic anterior uveitis (particularly in children), phthisis bulbi, silicone oil in the anterior chamber and severe chronic keratitis.
   b. ***Age-related*** band keratopathy is common and affects otherwise healthy individuals.
   c. ***Metabolic*** causes (metastatic calcification), which are rare, include increased serum calcium and phosphorus, hyperuricaemia and chronic renal failure.
   d. ***Hereditary*** causes include familial cases and ichthyosis.
2. **Signs** (in chronological order)
   - Peripheral interpalpebral calcification with clear cornea separating the sharp peripheral margins of the band from the limbus (Fig. 5.84).

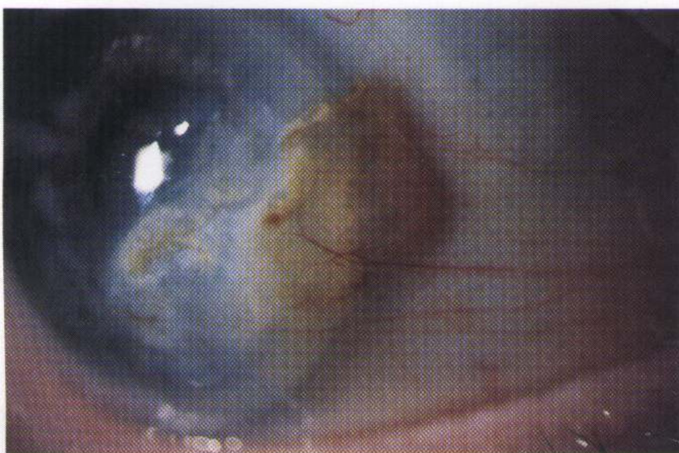

Fig. 5.83
Secondary lipid keratopathy


Fig. 5.84
Mild band keratopathy

• Gradual central spread to form a band-like chalky plaque containing transparent small holes and occasionally clefts (Fig. 5.85).



Fig. 5.85
Severe band keratopathy

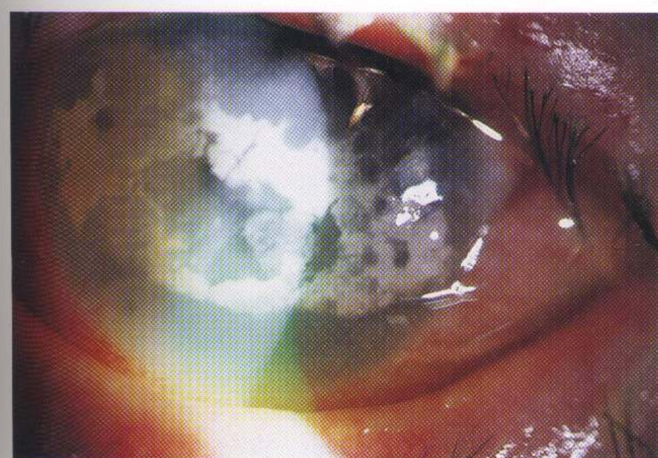


Fig. 5.86
Epithelial breakdown in longstanding band keratopathy

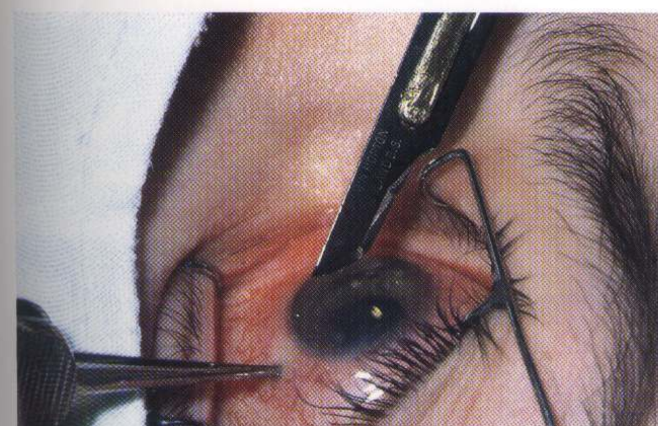


Fig. 5.87
Removal of corneal epithelium prior to chelation of band keratopathy

• Advanced lesions may become nodular and elevated with considerable discomfort due to epithelial breakdown (Fig. 5.86).

3. Treatment is indicated if vision is threatened or if the eye is uncomfortable.

a. Chelation is simple and effective for relatively mild cases and is performed under the microscope.
  - Large chips of calcium can be manually removed with forceps.
  - The corneal epithelium overlying the opacity and any solid layer of calcification are scraped off with a No. 15 blade (Fig. 5.87).
  - A solution of sodium versenate (edetate) is applied with a cotton-tipped bud until all calcium has been removed (Fig. 5.88).

b. Excimer laser keratectomy may be performed, if available.

> ***NB:*** It is important to recognize and treat any underlying conditions to prevent recurrences.

Spheroidal degeneration

Spheroidal degeneration has many eponyms, including corneal elastosis, Labrador keratopathy, climatic droplet keratopathy and Bietti nodular dystrophy. It is a bilateral, degenerative condition of unknown cause which typically occurs in men whose working lives are spent outdoors. The main postulated predisposing factor is ultraviolet exposure, since severity correlates closely with the length of time spent outdoors. The condition is relatively innocuous although visual impairment may occur rarely.

1. Signs (in chronological order)
  - Small, amber-coloured granules in the superficial stroma of the peripheral interpalpebral cornea.
  - Increasing opacification, coalescence and central spread.
  - Advanced lesions are nodular and the surrounding stroma often hazy (Fig. 5.89).

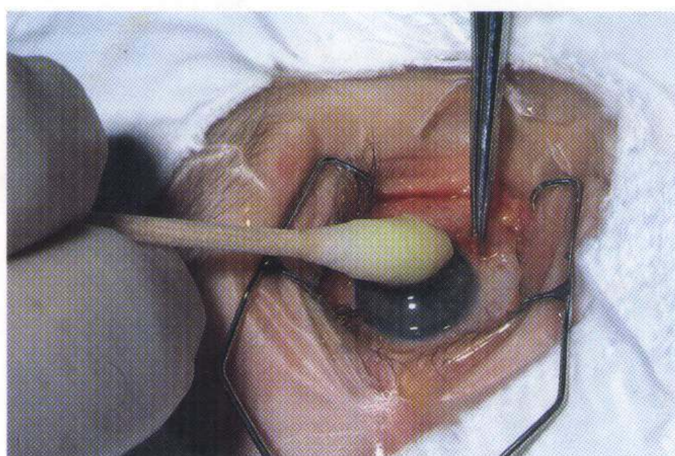
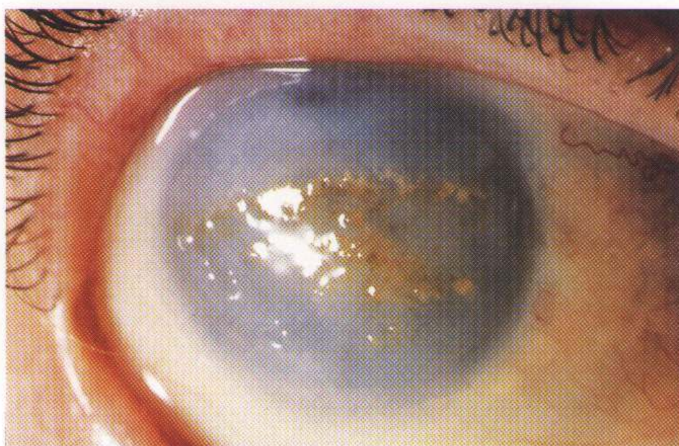


Fig. 5.88
Application of sodium versenate


Fig. 5.89
Spheroidal degeneration

2. **Treatment**
   a. ***Protection against ultraviolet damage*** with sunglasses.
   b. ***Superficial keratectomy*** to improve vision.
   c. ***Lamellar keratoplasty*** may be required for visually incapacitating cases.

Salzmann nodular degeneration

Salzmann nodular degeneration occurs secondary to chronic keratitis, especially trachoma.

1. **Signs**
   - Discrete, elevated grey or blue-grey, nodular, superficial stromal opacities (Fig. 5.90).
   - The lesions are located in scarred cornea or at the edges of transparent cornea.


Fig. 5.90
Salzmann nodular degeneration

   - The base of a nodule may be surrounded by epithelial iron deposits.
   - Recurrent epithelial erosions may occur.
2. **Treatment** is similar to that of spheroidal degeneration.

Corneal dystrophies

The corneal dystrophies are a group of progressive, usually bilateral, mostly genetically determined, non-inflammatory, opacifying disorders. The age at presentation varies between the first and fourth decades depending on the relative frequency of secondary recurrent epithelial erosions and visual impairment. Based on biomicroscopic and histopathological features, corneal dystrophies are classified into (a) *epithelial*, (b) *Bowman layer*, (c) *stromal* and (d) *endothelial*. Recent advances in molecular genetics have identified the responsible gene defects for most of the dystrophies.

Epithelial dystrophies

Epithelial basement membrane dystrophy

Also known as Cogan microcystic or map-dot-fingerprint dystrophy, this is the most common dystrophy seen in clinical practice, despite which it is frequently misdiagnosed due to its variable appearance. In contrast to other dystrophies it is neither familial nor progressive.

1. **Onset** is in the second decade. About 10% of patients develop recurrent corneal erosions in the third decade. The remainder are asymptomatic throughout life. Simultaneous bilateral recurrent erosions suggest epithelial basement membrane dystrophy.

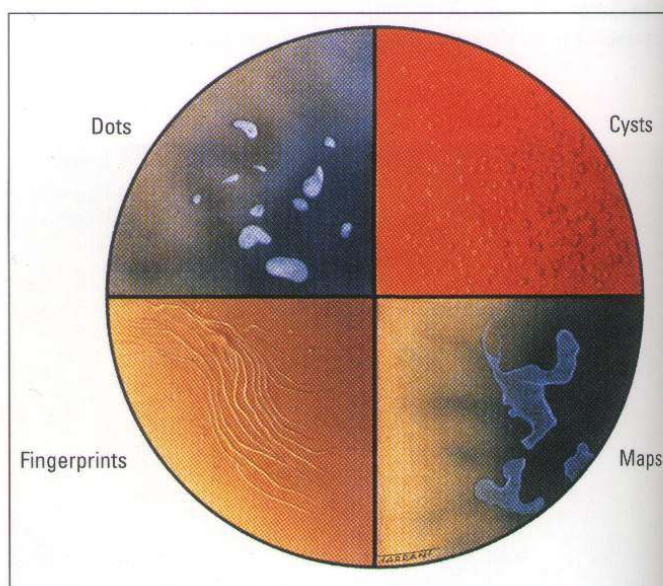


Fig. 5.91
Cogan dystrophy

2. **Signs**. The following lesions may be seen in isolation or combination and are best visualized by retroillumination or scleral scatter (Fig. 5.91).
   - Dot-like opacities (Fig. 5.92).
   - Epithelial microcysts (Fig. 5.93).
   - Subepithelial map-like patterns (Fig. 5.94).
   - Whorled fingerprint-like lines.

> *NB:* Over time one pattern frequently changes to another and the distribution of the lesions may also vary.

3. **Histology** shows thickening of the basement membrane with deposition of fibrillary protein between the basement membrane and Bowman layer. There is also absence of hemidesmosomes of the basal epithelial cells, which is responsible for recurrent corneal erosions.
4. **Treatment** is that of recurrent corneal erosions.

Meesmann dystrophy

1. **Inheritance** is autosomal dominant (AD) with the gene locus on 12q13 or 17q12.

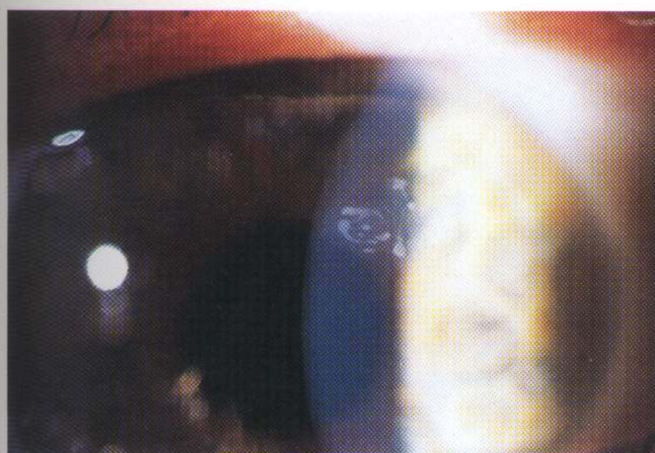


Fig. 5.92
Dot-like opacities in Cogan dystrophy



Fig. 5.93
Epithelial microcysts in Cogan dystrophy



Fig. 5.94
Subepithelial map-like patterns in Cogan dystrophy (Courtesy of J. Talks)

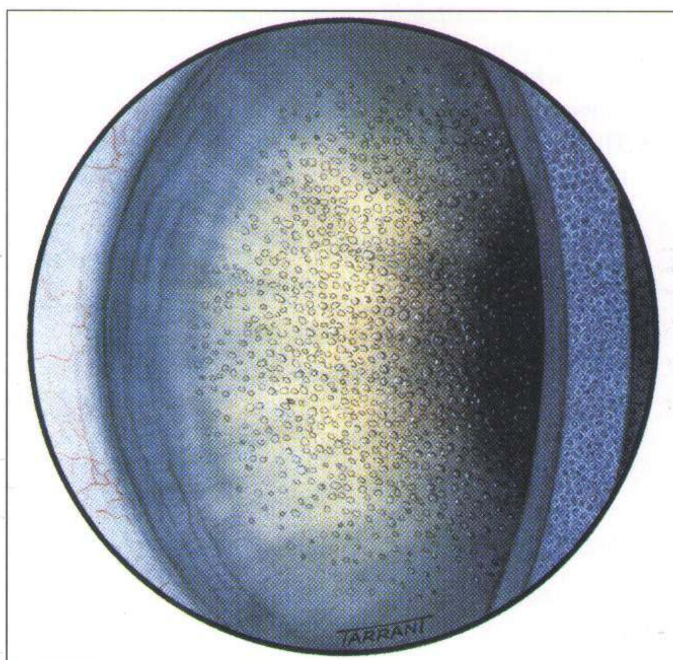


Fig. 5.95
Meesmann dystrophy

2. **Onset** of this very rare dystrophy is in the first 2 years of life with ocular irritation.
3. **Signs**. Myriads of tiny intraepithelial cysts of uniform size but variable density which are maximal centrally and extend towards but do not reach the limbus, which are best seen on retroillumination (Fig. 5.95).
4. **Histology** shows irregular thickening of the corneal epithelium with numerous vacuolated suprabasal cells.
5. **Treatment** is not normally required.

Bowman layer dystrophies

Reis–Bücklers dystrophy (Bowman layer type I)

1. **Inheritance** is AD with the gene locus on 5q31.
2. **Onset** is in early childhood with recurrent erosions.



Fig. 5.96
Reis–Bücklers dystrophy



Fig. 5.98
Schnyder dystrophy (Courtesy of K. Nischal)

3. **Signs**
   - Grey-white, fine, round and polygonal opacities in Bowman layer, most dense centrally (Fig. 5.96).
   - The changes increase in density with age, resulting in a reticular pattern due to the laying down of irregular bands of collagen replacing Bowman layer.
   - Corneal sensation is reduced and visual impairment may occur due to scarring at Bowman layer.
4. **Histology** shows that the new collagen stains blue with Masson trichrome, and Bowman layer is indistinct or absent.
5. **Treatment** is mainly by excimer laser keratectomy. Lamellar keratoplasty may be required in some cases but is associated with a high incidence of recurrence of the dystrophy on the graft, which may develop rapidly.

Thiel–Behnke dystrophy (Bowman layer type 2)

1. **Inheritance** is AD with the gene locus on 10q24.
2. **Onset** is at the end of the first decade with recurrent erosions.
3. **Signs** are similar to Reis–Bücklers dystrophy except that the opacities assume more of a honeycomb pattern (Fig. 5.97).
4. **Histology** is similar to Reis–Bücklers dystrophy.
5. **Treatment** may not be necessary because visual impairment is less than in Reis–Bücklers dystrophy.

Central Schnyder (crystalline) dystrophy

1. **Inheritance** is AD with the gene locus on 1p36–p34.1.
2. **Onset** is in the second decade with visual impairment, particularly with glare.
3. **Signs**. Central, oval area of scintillating, subepithelial 'crystalline' opacity in a generally hazy cornea (Fig. 5.98).
4. **Histology** shows deposits of phospholipid and cholesterol.
5. **Treatment** is by excimer laser keratectomy.

Stromal dystrophies

Lattice dystrophy type I (Biber–Haab–Dimmer)

1. **Inheritance** is AD with the gene locus on 5q31.
2. **Onset** is at the end of the first decade with recurrent erosions which precede typical stromal changes. It may therefore be initially missed.



Fig. 5.97
Thiel–Behnke dystrophy



Fig. 5.99
Mild lattice dystrophy type 1

3. **Signs** (in chronological order)
   - Anterior stromal dots.
   - Progression and coalescence into fine, spidery, branching lattice lines best seen on retroillumination (Fig. 5.99).
   - Deep and outward spread sparing the periphery (Fig. 5.99).
   - Generalized haze progressively impairs vision and may obscure the lattice lines (Fig. 5.100).
4. **Histology** shows amyloid which stains with Congo Red, exhibits metachromasia with Crystal Violet and birefringence under crossed polaroids.
5. **Treatment** by penetrating or deep lamellar keratoplasty is frequently required before the sixth decade.

Lattice dystrophy type 2 (Meretoja syndrome)

1. **Inheritance** is AD with the gene locus on 9q34.
2. **Onset** is in middle age with progressive facial palsy and corneal involvement. Recurrent erosions are less frequent than in type 1 lattice.
3. **Signs**. Randomly scattered, short, fine lattice lines which are sparse, more delicate and more radially orientated (Fig. 5.101) than in type 1 lattice dystrophy.
4. **Systemic features** include progressive bilateral cranial and peripheral neuropathy, dysarthria, dry and extremely lax itchy skin, a characteristic 'mask-like' facial expression, protruding lips and pendulous ears. Amyloidosis may also involve the kidneys and heart.
5. **Histology** shows amyloid deposits in the corneal stroma and other involved sites.
6. **Treatment** by penetrating or deep lamellar keratoplasty may be required in the seventh decade but may be complicated by recurrent infections consequent to exposure keratopathy.

Lattice dystrophy type 3 and 3A

1. **Inheritance** of type 3 is presumed to be autosomal recessive (AR) and that of type 3A is AD with the gene locus on 5q31 in both.
2. **Onset** is between the fourth and sixth decades with visual impairment but recurrent erosions are uncommon.
3. **Signs**
   - Thick, ropy lines extending from limbus to limbus with minimal intervening haze (Fig. 5.102).

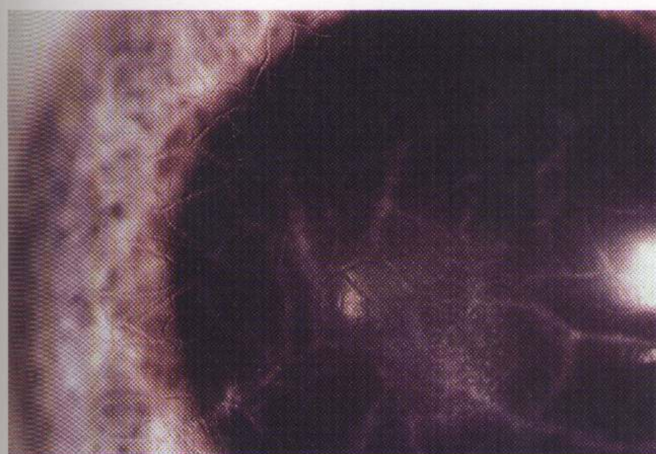


Fig. 5.100
Advanced lattice dystrophy type 1

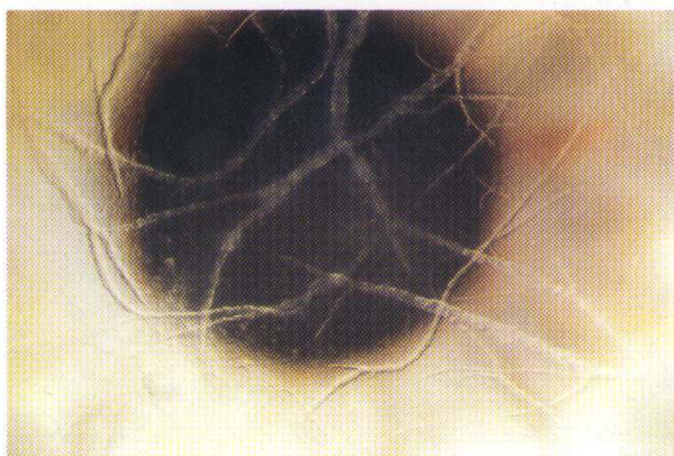


Fig. 5.102
Lattice dystrophy type 3

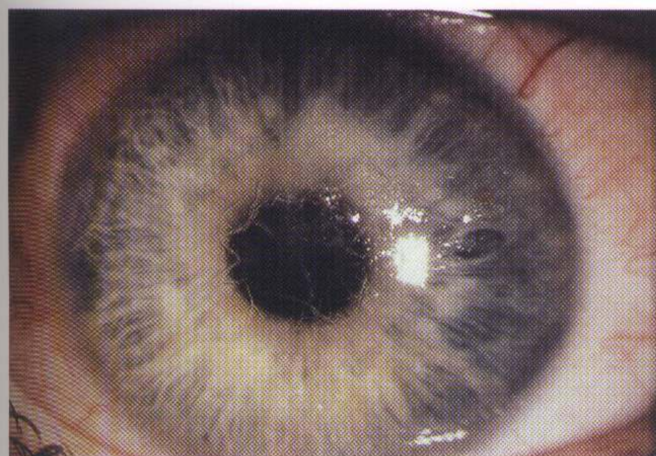


Fig. 5.101
Lattice dystrophy type 2



Fig. 5.103
Mild granular dystrophy (Courtesy of A. Ridgway)

- There may be gross asymmetry or the lesions may be unilateral for a time.
- Progression is rapid if the cornea is subjected to trauma, however minor.

4. **Treatment** by penetrating or deep lamellar keratoplasty is invariably required.

Granular dystrophy

1. **Inheritance** is AD with the gene locus on 5q31.
2. **Onset** is in the first decade with recurrent erosions.
3. **Signs** (in chronological order)
   - Small, white, sharply demarcated deposits resembling crumbs or snowflakes in the central anterior stroma (Fig. 5.103).
   - Increase in number of lesions with deeper and outward spread but not reaching the limbus (Fig. 5.104).
   - Gradual confluence causing impairment of visual acuity (Fig. 5.105).
4. **Histology** shows amorphous hyaline deposits which stain bright red with Masson trichrome.
5. **Treatment** by penetrating or deep lamellar keratoplasty is usually required by the fourth decade. Superficial recurrences may require repeated excimer laser keratectomy.

Avellino dystrophy

1. **Inheritance** is AD with the gene locus on 5q31.
2. **Onset** is in the first to second decades. Recurrent erosions are rare and, if present, mild, so that some patients may be unaware of their disease.
3. **Signs**. Superficial, fine, opacities that resemble rings, discs, stars or snowflakes, most dense centrally, resembling those seen in granular dystrophy associated with deeper linear opacities reminiscent of lattice dystrophy (Fig. 5.106).
4. **Histology** shows both hyaline and amyloid in the stroma.
5. **Treatment** is usually not required.

> *NB:* Avellino, granular and lattice type I dystrophies are linked to a single locus on chromosome 5q and may therefore represent different clinical forms of the same entity.

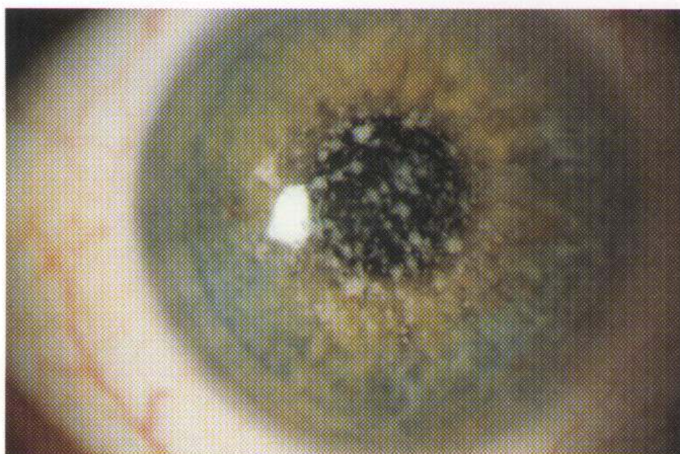


Fig. 5.104
Advanced granular dystrophy (Courtesy of A. Ridgway)



Fig. 5.106
Avellino dystrophy

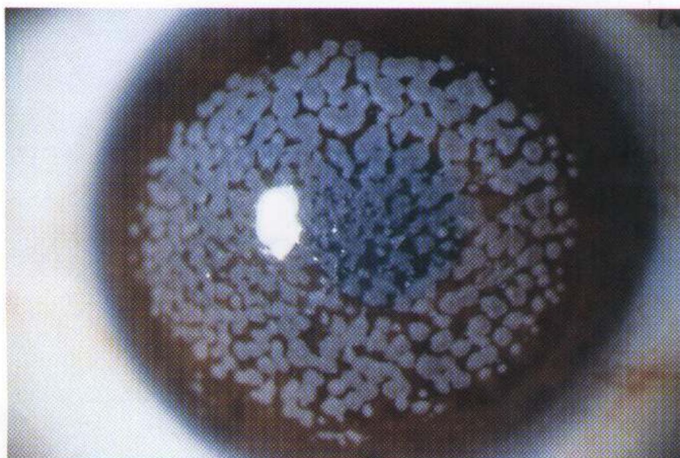


Fig. 5.105
Very severe granular dystrophy (Courtesy of A. Ridgway)

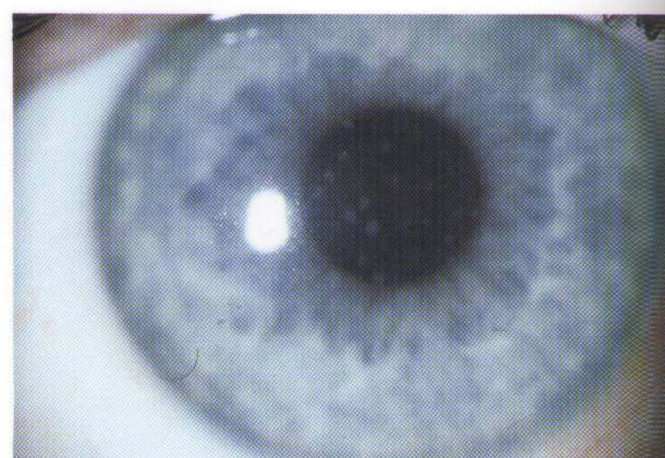


Fig. 5.107
Mild macular dystrophy (Courtesy of A. Ridgway)

Macular dystrophy

This is the least common stromal dystrophy in which a systemic inborn error of keratan sulphate metabolism has only corneal manifestations. It has been divided into types I, IA and II depending on the presence or absence of antigenic keratan sulphate (aKS) in the serum and cornea, though the corneal morphology is identical.

1. **Inheritance** is AR with the gene locus on 16q21.
2. **Onset** is towards the end of the first decade with gradual visual deterioration.
3. **Signs** (in chronological order)
   - Greyish-white, dense, focal, poorly delineated spots in the superficial cornea with mild diffuse stromal clouding (Fig. 5.107).
   - Increasing opacification (Fig. 5.108).
   - Eventual involvement of full-thickness stroma up to the limbus, associated with corneal thinning (Fig. 5.109).
4. **Histology** shows abnormally close packing of collagen in the corneal lamellae and abnormal aggregations of glycosaminoglycans which stain with Alcian Blue.

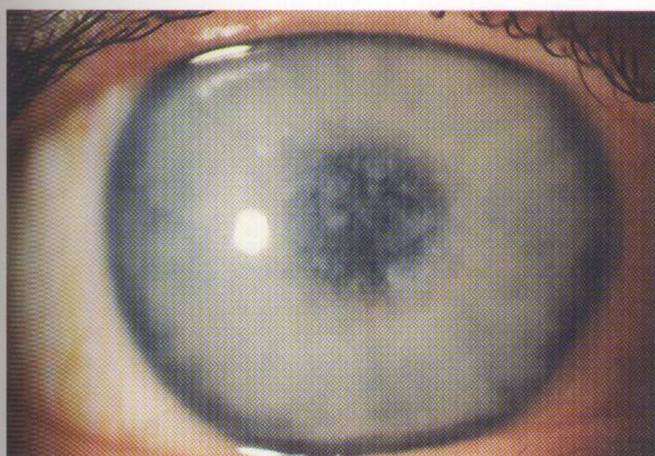


Fig. 5.108
Advanced macular dystrophy (Courtesy of A. Ridgway)



Fig. 5.109
Very severe macular dystrophy (Courtesy of A. Ridgway)

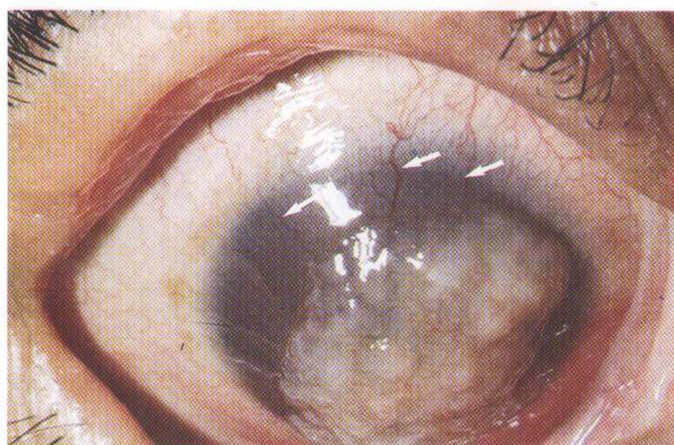


Fig. 5.110
Gelatinous drop-like dystrophy (Courtesy of T.A. Casey, K.W. Sharif, *Corneal Dystrophies and Degenerations*, Wolfe, 1991)

5. **Treatment** by penetrating keratoplasty is generally successful but late recurrence on the graft may occur.

Gelatinous drop-like dystrophy

This rare disorder is also known as familial subepithelial amyloidosis of the cornea.

1. **Inheritance** is AR.
2. **Onset** is in the first to second decades with severe photophobia, watering and visual impairment.
3. **Signs** (in chronological order)
   - Grey subepithelial nodules.
   - Gradual confluence, stromal involvement and increase in size giving rise to a nubbly, mulberry-like appearance (Fig. 5.110).
3. **Histology** shows subepithelial and anterior stromal accumulation of amyloid.
4. **Treatment** is with repeated superficial keratectomy because of early recurrences on corneal grafts.

Endothelial dystrophies

Fuchs endothelial dystrophy

Fuchs endothelial dystrophy is more common in women and is associated with a slightly increased prevalence of primary open-angle glaucoma.

1. **Inheritance** may occasionally be AD although the majority are sporadic.
2. **Onset** of this slowly progressive disease is in old age.
3. **Signs** (in chronological order)
   a. *Stage 1* is characterized by a gradual increase of central guttata with peripheral spread and confluence, giving rise to a 'beaten-metal' appearance (Fig. 5.111).
   b. *Stage 2* is characterized by endothelial decompensation resulting in central stromal oedema and blurred vision, initially worse in the morning, which clears later in the

day. Epithelial oedema develops when stromal thickness has increased by about 30% (Fig. 5.112).

c. Stage 3 is characterized by persistent epithelial oedema and results in bullae (bullous keratopathy) (Fig. 5.113) which cause pain and discomfort on rupture, due to exposure of naked nerve endings. Replacement of Bowman layer by a degenerative pannus and gradual stromal opacification supervene.



Fig. 5.111
'Beaten-metal' appearance in early Fuchs endothelial dystrophy

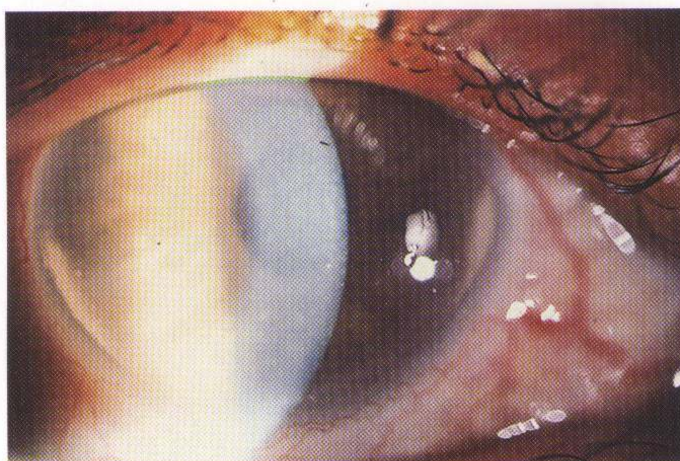


Fig. 5.112
Corneal epithelial oedema in Fuchs endothelial dystrophy



Fig. 5.113
Bullous keratopathy in advanced Fuchs endothelial dystrophy

4. Treatment

a. Hypertonicity of the tear film may be achieved by sodium chloride 5% drops or ointment or simple measures such as a hair dryer. This may be effective in 'dehydrating' early epithelial oedema.

b. Bandage contact lenses provide comfort by protecting exposed nerve endings and flattening bullae.

c. Penetrating keratoplasty has a high success rate and should not be delayed.

d. Other options in eyes with poor visual potential include conjunctival flaps and amniotic membrane transplants.

Posterior polymorphous dystrophy

This is a rare, innocuous and asymptomatic dystrophy in which corneal endothelial cells display characteristics similar to epithelium.

1. **Inheritance** is usually AD with the gene locus on chromosome 20.
2. **Onset** is at birth or soon thereafter, although is most frequently identified by chance in later life.
3. **Signs** (Fig. 5.114), which are subtle, consist of vesicular (Fig. 5.115), band-like (Fig. 5.116) or geographic endothelial patterns which may be asymmetrical.
4. **Associations** include iris membranes, peripheral anterior synechiae, ectropion uveae, corectopia and glaucoma reminiscent of iridocorneal endothelial syndrome (*see* Chapter 9). It has therefore been speculated that the two clinical pictures may represent points on a spectrum of

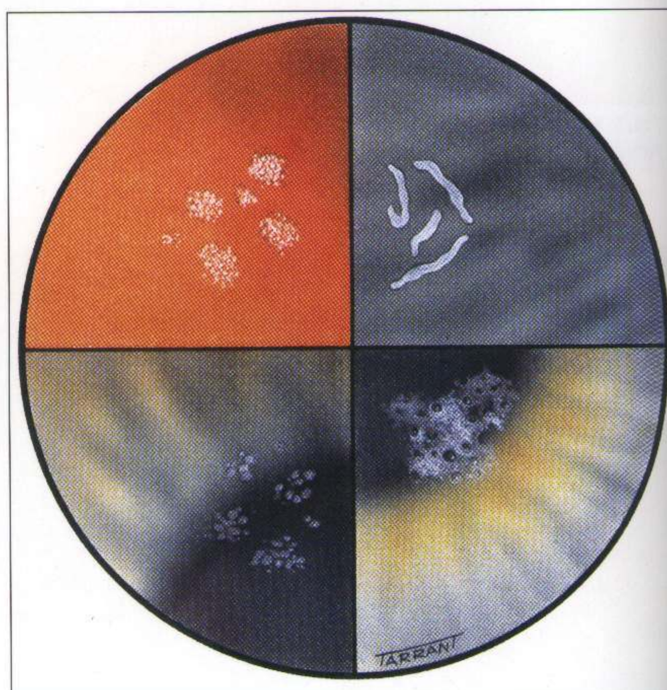


Fig. 5.114
Posterior polymorphous dystrophy

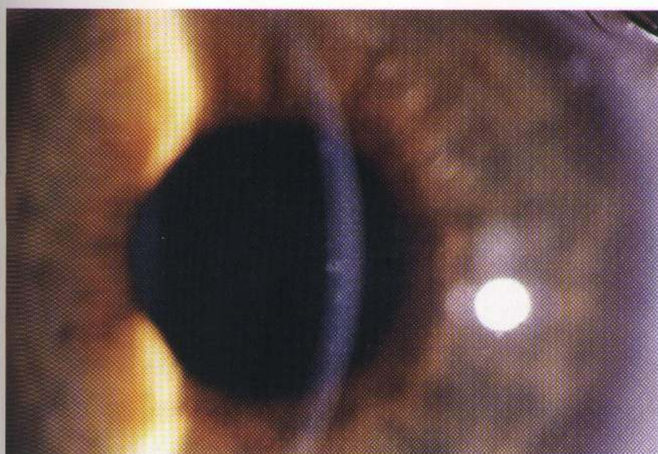

Fig. 5.115
Vesicular lesions in posterior polymorphous dystrophy


Fig. 5.116
Band-like lesion in posterior polymorphous dystrophy

one disease. There is also an association with Alport syndrome.

5. Treatment is not required.

Congenital hereditary endothelial dystrophy (CHED)

This is a rare dystrophy in which there is focal or generalized absence of corneal endothelium. There are two main forms, CHED1 and CHED2, the latter being more severe.

1. Inheritance

a. CHED1 is autosomal dominant with the gene locus on 20p11.2–q11.2.

b. CHED2 is autosomal recessive with the gene locus on 20p13.

2. Onset is at or shortly after birth.

3. Signs

- Bilateral, symmetrical, diffuse corneal oedema.
- Corneal appearance varies from a blue-grey, ground-glass appearance (Fig. 5.117) to total opacification.

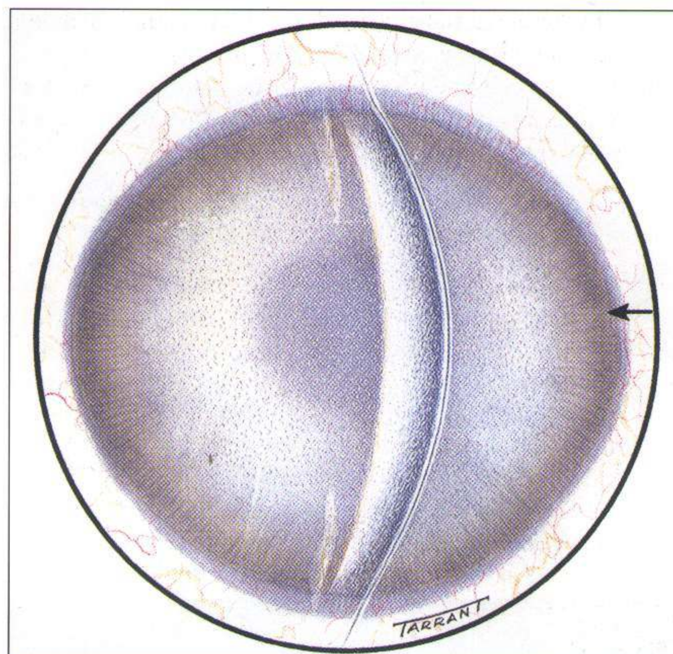


Fig. 5.117
Congenital hereditary endothelial dystrophy (Courtesy of T.A. Casey, K.W. Sharif, *Corneal Dystrophies and Degenerations*, Wolfe, 1991)

- Visual impairment is variable; acuity may surpass that expected from corneal appearance.

4. Differential diagnosis includes other causes of neonatal corneal opacification such as congenital glaucoma, mucopolysaccharidoses, birth trauma, rubella keratitis and sclerocornea.

5. Treatment by penetrating keratoplasty has a reasonable chance of success when performed early but is risky and technically more difficult than that in adults. Undue delay in surgical intervention carries the risk of dense amblyopia.

Corneal ectasias

Keratoconus

Keratoconus is a progressive disorder in which the cornea assumes an irregular conical shape. The onset is at around puberty with slow progression thereafter, though the ectasia may become stationary at any time. Both eyes are affected, if only topographically, in almost all cases. The role of heredity has not been clearly defined and most patients do not have a positive family history. Offspring appear to be affected in only about 10% of cases and AD transmission with incomplete penetrance has been proposed.

Associations

1. Systemic disorders include Down, Turner, Ehlers–Danlos and Marfan syndromes, atopy, osteogenesis imperfecta and mitral valve prolapse.

2. **Ocular associations** include vernal keratoconjunctivitis, blue sclera, aniridia, ectopia lentis, Leber congenital amaurosis and retinitis pigmentosa. Rigid contact lens wear and constant eye rubbing have also been proposed as predisposing factors.

Classification according to morphology

1. **Nipple cones** are characterized by small size (5 mm) and steep curvature (Fig. 5.118). The apex is central or paracentral and displaced inferonasally.
2. **Oval cones** are larger (5–6 mm), ellipsoid and commonly decentred inferotemporally (Fig. 5.119).
3. **Globus cones** are the largest (>6 mm) and may involve over 75% of the cornea (Fig. 5.120).

In mild cases cone morphology may be indeterminate.



Fig. 5.118
Nipple cone in keratoconus

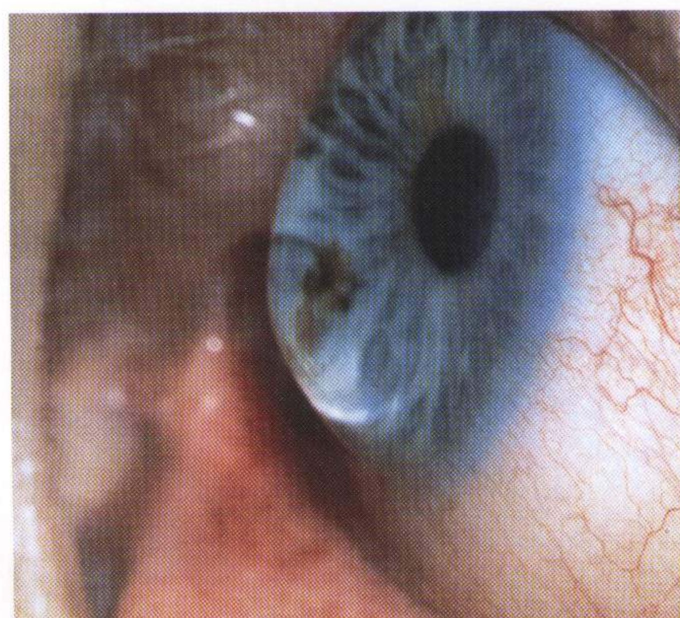


Fig. 5.119
Oval cone in keratoconus (Courtesy of R. Visser)



Fig. 5.120
Globus cone in keratoconus

Presentation

This is with unilateral impairment of vision due to progressive myopia and astigmatism, which subsequently becomes irregular. The patient may report frequent changes in spectacle prescription or decreased tolerance to contact lens wear. As a result of the asymmetrical nature of the condition, the fellow eye usually has normal vision with negligible astigmatism at presentation, which however, increases as the condition progresses.

Signs

The hallmark of keratoconus is central or paracentral stromal thinning, apical protrusion and irregular astigmatism. It can be graded by keratometry according to severity as mild (<48 D), moderate (48–54 D) and severe (>54 D).



Fig. 5.121
'Oil-droplet' reflex in keratoconus

1. **Early signs**, often subtle, can be detected as follows:
   - Direct ophthalmoscopy from a distance of one foot shows an 'oil droplet' reflex (Fig. 5.121).
   - Retinoscopy shows an irregular 'scissor' reflex.
   - Slit-lamp biomicroscopy shows very fine, vertical, deep stromal striae (Vogt lines) which disappear with external pressure on the globe (Fig. 5.122).
   - Prominent corneal nerves may also be present.
   - Keratometry shows irregular astigmatism where the principal meridia are no longer 90° apart and the mires cannot be superimposed.
   - Corneal topography is the most sensitive method for detecting very early keratoconus (Fig. 5.123).
2. **Late signs**
   - Progressive corneal thinning, to as little as one-third of normal thickness, associated with poor visual acuity resulting from marked irregular myopic astigmatism with steep keratometry (K) readings.

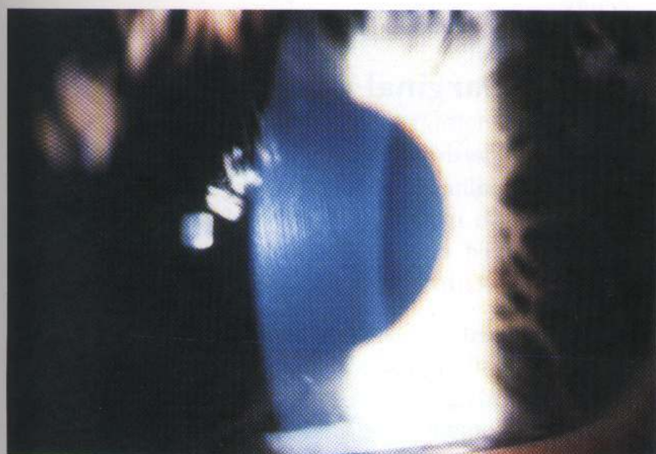


Fig. 5.122
Vogt striae in keratoconus



Fig. 5.124
Munson sign in keratoconus

   - Bulging of the lower lid in downgaze (Munson sign) (Fig. 5.124).
   - Epithelial iron deposits (Fleischer ring) may surround the base of the cone and are visualized best with a cobalt blue filter.
   - Stromal scarring in severe cases (Fig. 5.125).
3. **Acute hydrops** is an acute influx of aqueous into the cornea as a result of a rupture in Descemet membrane (Fig. 5.126). This causes a sudden drop in visual acuity associated with discomfort and watering. Although the break usually heals within 6–10 weeks and the corneal oedema clears, a variable amount of stromal scarring may develop. Acute episodes are initially treated with hypertonic saline and patching or a soft bandage contact lens. Healing may result in improved visual acuity as a result of scarring and flattening of the cornea. Keratoplasty should be deferred until the oedema has resolved.

Management

1. **Spectacles** in early cases to correct regular and mild irregular astigmatism.

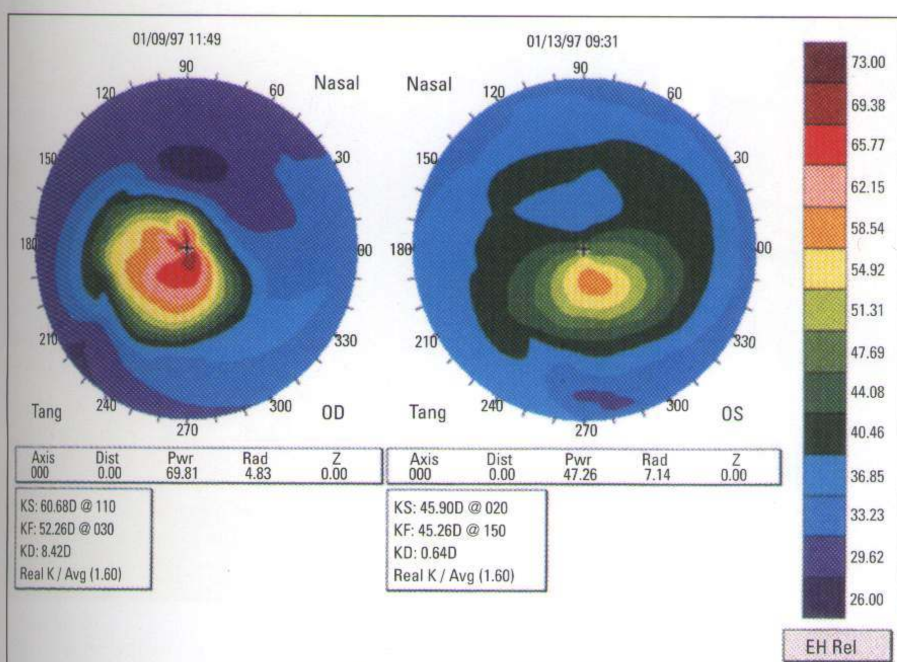


Fig. 5.123
Relative scale corneal maps showing advanced keratoconus in the right eye and an early paracentral cone in the left eye
(Courtesy of E. Morris)

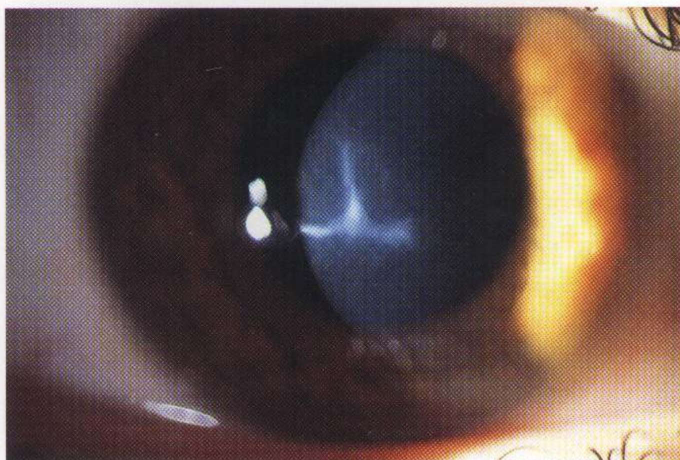

Fig. 5.125
Apical corneal scarring in advanced keratoconus


Fig. 5.126
Acute hydrops in keratoconus

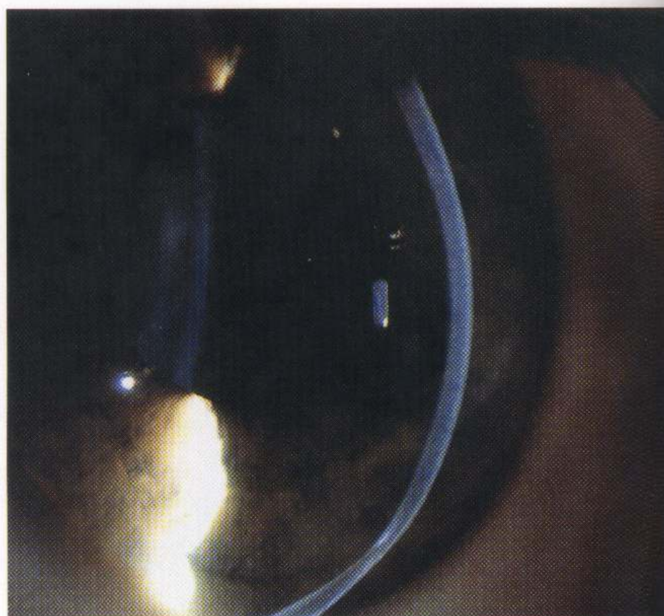

Fig. 5.127
Corneal scarring in keratoconus

2. **Rigid contact lenses** are required for higher degrees of astigmatism and provide a regular refracting surface. Advances in both lens design and material have increased the proportion of keratoconus patients who can use contact lenses. The following types of contact lenses can be used:
   - Standard, large diameter (9.7 mm), gas-permeable lenses in early cases.
   - Aspherical lenses for moderate nipple cones.
   - Small steep lenses for moderate to severe nipple cones.
   - Specially designed lenses for steep oval and globus cones when standard spherical lenses have failed.
   - Gas-permeable scleral lenses can be tried in extremely distorted corneas or very sensitive eyes which cannot tolerate corneal diameter contact lenses.
3. **Epikeratoplasty** is effective in patients intolerant to contact lenses without significant central corneal scarring.
4. **Keratoplasty**, penetrating or deep lamellar, is indicated in patients with advanced progressive disease, especially with significant corneal scarring (Fig. 5.127). Although clear grafts are obtained in over 85% of cases, optical outcomes may be compromised by residual astigmatism and anisometropia, necessitating contact lens correction for best acuity.

Pellucid marginal degeneration

Pellucid marginal degeneration is a rare condition which may be initially misdiagnosed as keratoconus, although occasionally the two may coexist and some patients may have atopy. Advanced cases with marked protrusion may be difficult to differentiate from keratoconus.

1. **Presentation** is in the third to fifth decades with increasing astigmatism.
2. **Signs**
   - Bilateral, slowly progressive, crescent-shaped band of inferior corneal thinning extending from 4 to 8 o'clock (Fig. 5.128).


Fig. 5.128
Pellucid marginal degeneration (Courtesy of R. Visser)

- The area of thinning usually measures 1–2 mm in width and is separated from the limbus by normal cornea.
- The central cornea protrudes above the area of thinning, flattening in the vertical meridian with severe irregular against-the-rule astigmatism.
- Unlike keratoconus Fleischer rings and Vogt striae do not occur, but epithelial oedema may develop in the inferior cornea in advanced cases.

3. **Management**
   a. *Spectacles* usually fail very early as irregular astigmatism increases.
   b. *Gas-permeable* scleral lenses are often the best option.
   c. *Surgical options,* none of which are ideal, in patients intolerant to contact lenses include wedge resection of diseased tissue, large penetrating keratoplasty, crescentic lamellar keratoplasty and thermokeratoplasty.

Keratoglobus

Keratoglobus is an extremely rare condition in which the entire cornea is abnormally thin. Possibly related to keratoconus, it may be associated with Leber congenital amaurosis and blue sclerae.

1. **Onset** is at birth.
2. **Signs**
   - In contrast with keratoconus the cornea develops globular, rather than conical ectasia.
   - Corneal thinning is generalized rather than at the apex of the protrusion (Fig. 5.129).
   - Acute hydrops occurs less commonly than in either keratoconus or pellucid marginal degeneration but the cornea is more prone to rupture on relatively mild trauma.
3. **Management** is with scleral contact lenses because the results of surgery are very poor.



Fig. 5.129
Keratoglobus

Neurokeratopathies

Neuroparalytic (exposure) keratopathy

This is the result of improper wetting of the ocular surface by the tear film because of inability to close the eyes on blinking (lagophthalmos), despite normal tear production.

1. **Causes** include facial nerve palsy, severe proptosis and scarring of the eyelids. The patient with a weak Bell phenomenon is at particular risk. Occasionally, corneal exposure during sleep may occur in normal individuals.
2. **Signs** range from mild inferior punctate epithelial changes (Fig. 5.130) to severe ulceration (Fig. 5.131).
3. **Treatment** if recovery is anticipated, involves frequent instillation of lubricants during the day and ointment and taping shut of the eyelids at night. If permanent, lid surgery is usually required (*see* Chapter 1).



Fig. 5.130
Inferior epithelial changes in neuroparalytic keratopathy

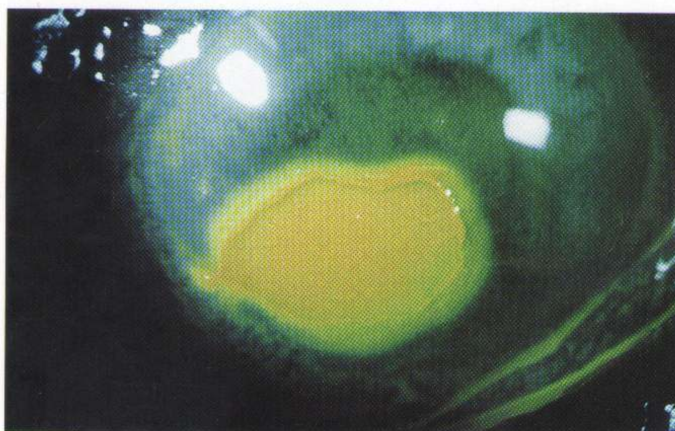


Fig. 5.131
Corneal ulcer in neuroparalytic keratopathy stained with fluorescein

Neurotrophic keratopathy

This occurs in an anaesthetic cornea. Although the pathogenesis is unclear, it appears that sensory innervation is vital to the health of the corneal epithelium. The loss of neural influences causes intracellular oedema, exfoliation of the epithelial cells and impairment of epithelial healing, culminating in persistent and progressive ulceration.

1. **Causes**
   a. ***Acquired*** causes include section of the fifth nerve, herpes simplex and zoster keratitis, diabetes, leprosy, acoustic neuroma and abuse of topical anaesthetics.
   b. ***Congenital*** causes include familial dysautonomia (Riley–Day syndrome), anhidrotic ectodermal dysplasia and congenital insensitivity to pain.
2. **Signs** tend to wax and wane, some patients developing serious lesions early and others after many years. In order of severity the corneal changes are as follows:
   - Grey, slightly opaque and oedematous epithelium (Fig. 5.132).
   - Punctate epithelial erosions most marked in the interpalpebral area.
   - Slow-healing epithelial defects which may become infected.
   - Stromal corneal melting and perforation are uncommon (Fig. 5.133).
3. **Prevention** involves the induction of protective ptosis by injection of botulinum toxin into the levator muscle, 3 days before any neurosurgical procedure on the trigeminal nerve to allow time for full effect. If toxin is not available, tarsorrhaphy should be performed.
4. **Treatment** of established keratopathy is aimed at promoting re-epithelialization with lubricants and patching. Other recently described treatment modalities include topical nerve growth factor drops and amniotic membrane transplantation.



Fig. 5.132
Epithelial changes in mild neurotrophic keratopathy

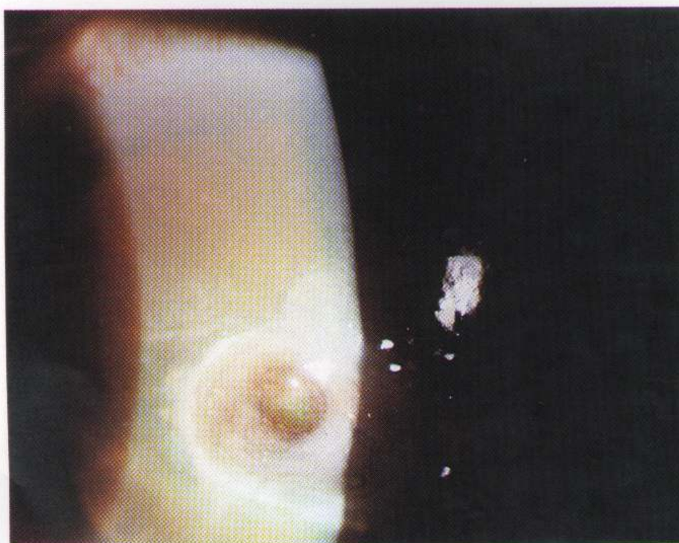


Fig. 5.133
Corneal perforation in neurotrophic keratopathy

Recurrent corneal erosion syndrome

The recurrent corneal erosion syndrome is a distressing condition characterized by disturbance of the epithelial basement membrane resulting in defective adhesion and recurrent breakdown of the epithelium. The condition most commonly follows superficial corneal trauma, especially a scratch. It may also occur in certain corneal dystrophies, particularly epithelial basement membrane dystrophy, as already described. Recurrent corneal erosions tend to be particularly troublesome in diabetic patients.

Clinical features

1. **Presentation** is typically on waking with sudden pain, lacrimation, photophobia and blurred vision, which usually resolve spontaneously within a few hours. Some patients experience several recurrences until normal attachment of the basal layer of the epithelium is restored.

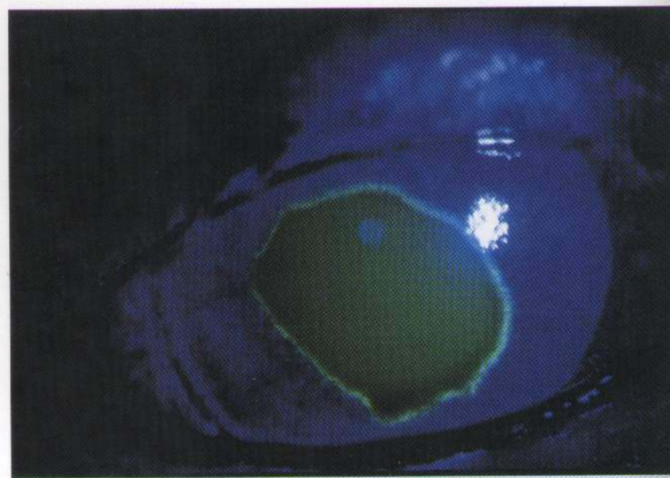


Fig. 5.134
Traumatic corneal macroerosion stained with fluorescein

2. **Signs**
   a. *Microerosions* are spontaneous small epithelial defects, associated with epithelial basement membrane dystrophy, which cause relatively mild symptoms.
   b. *Macroerosions* are extremely painful large epithelial defects with surrounding loosely adherent epithelium, most commonly associated with previous trauma (Fig. 5.134). Abrasions caused by a fingernail are particularly likely to progress to recurrent erosions.

> *NB:* It is important to examine the fellow eye for evidence of corneal dystrophy.

Treatment of acute erosions

1. **Topical** treatment is with lubricants while the epithelium is healing. A mild cycloplegic (e.g. cyclopentolate) and a non-steroidal anti-inflammatory agent (e.g. ketorolac tromethamol 0.5%) may increase patient comfort.

> *NB:* Although pressure patching has been standard treatment in the past it has become apparent that the cornea heals faster and the patient has less pain when it is not applied.

2. **Debridement** is indicated in severe cases with extensive devitalization and disadhesion of the epithelium. It is performed as follows:
   a. The zone of defective adhesion is determined by anaesthetizing the cornea and then touching the involved area with a sterile moistened cotton-tipped bud.
   b. Abnormal epithelium will become loose with minimal pressure and take on a grey colour.
   c. Debridement is then accomplished by first gently scrubbing the loose epithelium with a cellulose sponge and then removing it with small forceps.
   d. Instillation of cyclopentolate 1% and antibiotic ointment.

Prophylactic treatment

This should be considered in patients with frequent or severe recurrences.

1. **Topical lubricants** four times daily and at night for 8 weeks is usually effective for relatively mild cases.
2. **Extended-wear bandage contact lenses** with a low water content are useful if lubrication is ineffective. Lens wear has to be continued for 2 months until epithelial re-adhesion has occurred.
3. **Epithelial keratectomy** may be necessary for severe recalcitrant cases, particularly when associated with aberrant basement membrane in corneal dystrophies and degenerations. The procedure can be performed with an excimer laser (phototherapeutic keratectomy) or a Bard–Parker knife and involves removal of the entire epithelium which takes 5–7 days to regrow.
4. **Anterior stromal micropuncture** is an alternative treatment for recalcitrant post-traumatic erosions, for focal and peripheral lesions. It is performed at the slit-lamp and involves making multiple anterior stromal micropunctures with a bent 25-gauge needle. This incites focal microcicatrization with more secure epithelial adhesion. Treatment to the visual axis should be avoided if possible.
5. **Systemic tetracycline** 250 mg b.d. for 12 weeks may also be helpful. The mechanism of action is not fully understood and is probably not related to its antibacterial properties.

Drug-induced keratopathies

Chrysiasis

Chrysiasis is the deposition of gold in living tissue, occurring after prolonged administration of gold, usually in the treatment of rheumatoid arthritis. Virtually all patients on continuous chrysotherapy who have received a total dose of gold compound exceeding 1000 mg develop corneal deposits. Corneal chrysiasis is characterized by dust-like or glittering purple granules throughout the corneal stroma, more concentrated in the deep layers and the periphery. These findings are innocuous and therefore not an indication for cessation of therapy. Visually inconsequential lens deposits also develop in about 50% of patients treated for 3 or more years.

Vortex keratopathy

Vortex keratopathy (cornea verticillata) is characterized by whorl-like corneal epithelial deposits.

1. **Signs** (in chronological order)
   - Bilateral, fine greyish or golden-brown opacities in the inferior corneal epithelium.
   - Arborizing horizontal lines in a pattern resembling cat's whiskers, similar to the more common Hudson–Stahli line.

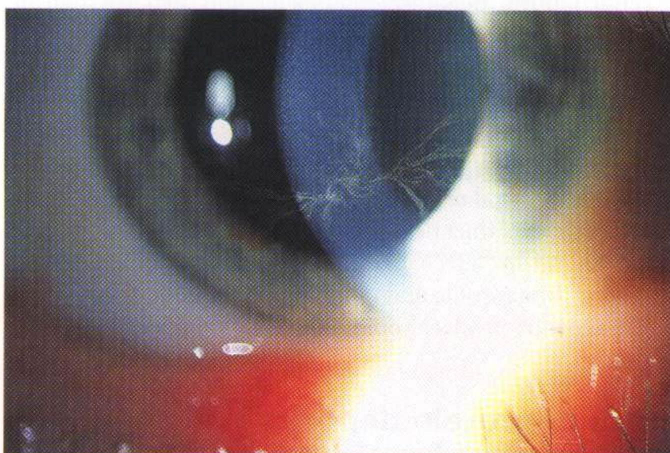


Fig. 5.135
Vortex keratopathy

- A whorl-like pattern which originates from a point below the pupil and swirls outwards, sparing the limbus (Fig. 5.135).

> *NB:* Although deposits may involve the visual axis, vision is not impaired but some patients may experience haloes around lights.

2. Causes

a. Antimalarials (chloroquine and hydroxychloroquine) are common causes. Unlike retinopathy, keratopathy bears no relationship to dosage or duration of treatment. The changes are usually reversible on cessation of therapy, although they may clear despite continued administration.

b. Amiodarone is a drug used to treat cardiac arrhythmias. Virtually all patients on amiodarone develop keratopathy, which is reversible on discontinuation of medication. In general the higher the dose and the longer the duration of administration, the more advanced the corneal deposits. Visually inconsequential anterior subcapsular lens deposits also develop in about 50% of patients on moderate to high doses. Optic neuropathy is a rare complication.

> *NB:* Vortex keratopathy also occurs in Fabry disease, which is a glycolipidosis caused by deficiency of the enzyme alpha-galactosidase A. Systemic features include angiokeratomas, cardiovascular and renal disease. Spoke-like lens opacities may also be present.

Metabolic keratopathies

Cystinosis

Cystinosis is a rare, AR, metabolic disorder characterized by widespread tissue deposition of non-protein cystine crystals as a result of a defect in lysosomal transport.

1. **Systemic features** include severe growth retardation, renal failure, hepatosplenomegaly and hypothyroidism. Patients with the most severe nephropathic form usually succumb before the second decade.
2. **Ocular features** are characterized by progressive deposition of cystine crystals in the conjunctiva and cornea which cause intense photophobia, blepharospasm, epithelial erosions and visual disability. Peripherally, crystals involve the entire stromal thickness, whereas centrally only the anterior two-thirds are affected (Fig. 5.136). Later, involvement of the iris, lens capsule and retina further affects vision.
3. **Treatment** involves topical 0.2% cysteamine for several weeks.

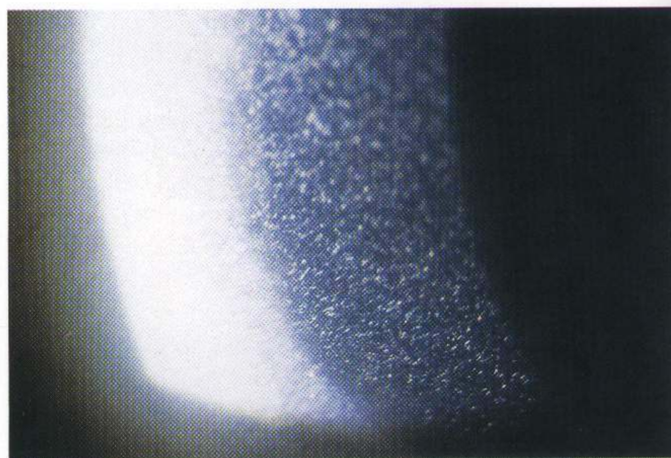


Fig. 5.136
Corneal crystals in cystinosis

Immunoprotein deposits

Diffuse or focal immunoprotein deposition is a relatively uncommon manifestation of several systemic diseases, including multiple myeloma, Waldenström macroglobulinaemia, monoclonal gammopathy of unknown cause, certain lymphoproliferative disorders and leukaemia. Corneal involvement may be the earliest manifestation of the disease.



Fig. 5.137
Corneal crystals in monoclonal gammopathy

1. **Signs**. Gradual bilateral development of a band of multiple, punctate, flake-like opacities mostly at the level of the posterior stroma (Fig. 5.137).
2. **Treatment** should address the underlying systemic disease with cytotoxic chemotherapy or steroids. Severe corneal involvement may require penetrating keratoplasty.

Mucopolysaccharidoses

The mucopolysaccharidoses (MPS) are a group of inherited deficiencies of catabolic glycosidases necessary for hydrolysis of mucopolysaccharides. The altered metabolite accumulates in intracellular vacuoles in various tissues and organs and is also detectable in the urine.



Fig. 5.138
Facial coarseness in Hurler syndrome



Fig. 5.139
Corneal clouding in Hurler syndrome

1. **Inheritance** is AR with the exception of the two subtypes of Hunter disease which are X-linked recessive.
2. **Systemic features**, which vary with the type of MPS, include facial coarseness (Fig. 5.138), skeletal anomalies, mental retardation and heart disease.
3. **Corneal deposits** are generally associated with skeletal anomalies and occur in all MPS except Hunter and Sanfilippo. In Hurler and Scheie they are most severe (Fig. 5.139) and present at birth. Corneal clouding in this setting should be differentiated from that secondary to congenital glaucoma, rubella keratopathy, congenital hereditary endothelial dystrophy and birth trauma.
2. **Other ocular features**
   a. *Pigmentary retinopathy* occurs in all except Morquio and Maroteaux–Lamy.
   b. *Optic atrophy* occurs in all six MPS and is most severe in Hurler.
   c. *Glaucoma* is rare.

Wilson disease

Wilson disease (hepatolenticular degeneration) is a rare condition caused by a deficiency of caeruloplasmin. It is characterized by a widespread deposition of copper in the tissues.

1. **Presentation** is with liver disease, basal ganglia dysfunction or psychiatric disturbances.
2. **Corneal deposits** of copper are present in nearly all patients. The classic Kayser–Fleischer ring, located at the peripheral part of Descemet membrane, appears as a zone of granules which change colour under different types of illumination (Fig. 5.140). The copper is deposited preferentially in the vertical meridian and may disappear with penicillamine therapy.

> *NB:* An early Kayser–Fleischer ring is best detected on gonioscopy.

3. **Anterior capsular green 'sunflower' cataract** is seen in some patients.

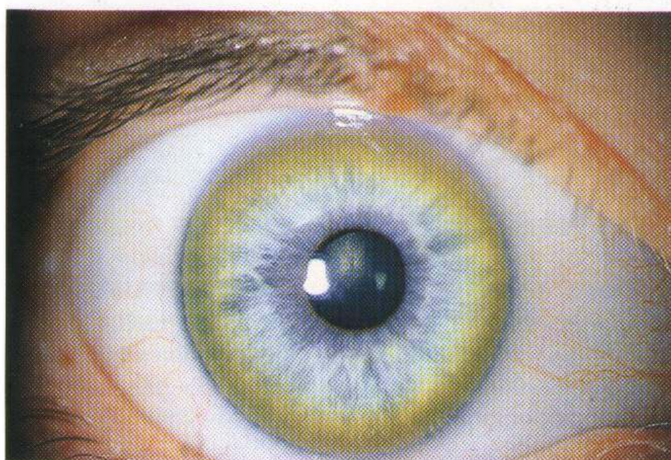


Fig. 5.140
Kayser–Fleischer ring in Wilson disease (Courtesy of R. Chopdar)

Congenital corneal anomalies

Microcornea

This is a rare unilateral or bilateral condition. Inheritance is usually AD.

1. **Signs**. The adult horizontal corneal diameter is 10 mm or less, the anterior chamber is shallow but other dimensions normal (Fig. 5.141).

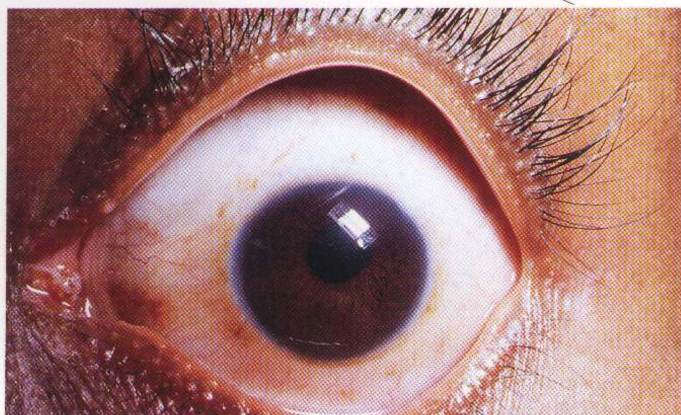


Fig. 5.141
Microcornea (Courtesy of J. Salmon)

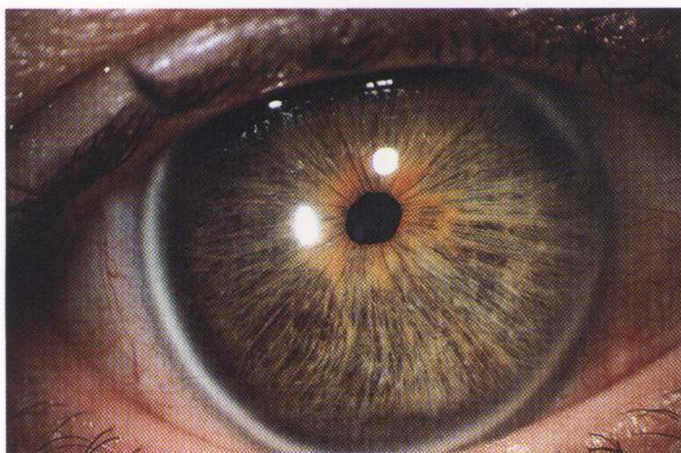


Fig. 5.142
Megalocornea

2. **Ocular associations** include glaucoma (initially closed and later open angle), congenital cataract, cornea plana, leukoma, iris abnormalities, microphakia, optic nerve hypoplasia and hypermetropia.
3. **Systemic associations** include fetal alcohol, Turner, Ehlers–Danlos, Weill–Marchesani, Waardenburg, Nance–Horan and Cornelia de Lange syndromes.

Megalocornea

This is a rare, bilateral, non-progressive enlargement of the cornea affecting males which must not be confused with buphthalmos due to congenital glaucoma. Inheritance is X-linked recessive.

1. **Signs**. Corneal diameter 13 mm or more, very deep anterior chamber, high myopia and astigmatism but normal visual acuity (Fig. 5.142). Lens subluxation may occur due to zonular stretching.
2. **Systemic associations** include Marfan, Apert, Ehlers–Danlos and Down syndromes, osteogenesis imperfecta, progressive facial hemiatrophy, renal carcinoma and mental handicap.

Cornea plana

This is a rare bilateral condition.

1. **Signs**. Severe decrease of corneal curvature (K readings 20–30 D), hypermetropia, shallow anterior chamber and a predisposition to angle closure glaucoma (Fig. 5.143).
2. **Ocular** associations include microcornea, sclerocornea, microphthalmos and Peters anomaly.

Posterior keratoconus

This is an uncommon, unilateral, non-progressive increased curvature of the posterior corneal surface. The anterior corneal surface is normal. Due to similar refractive indices of cornea and aqueous humour vision is minimally affected unless corneal clouding is present. Posterior keratoconus is divided into two types:

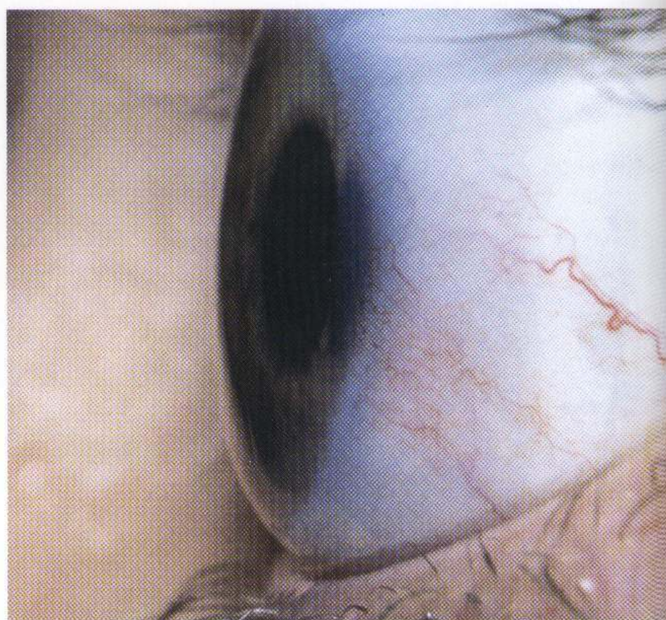


Fig. 5.143
Cornea plana (Courtesy of R. Visser)

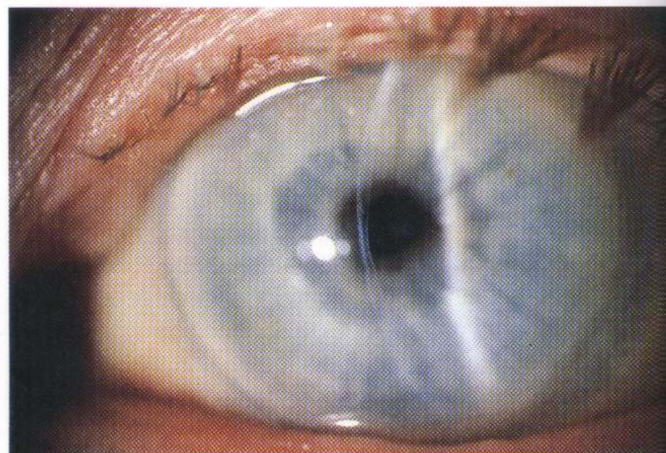


Fig. 5.144
Posterior keratoconus (Courtesy of S. Johns)

1. **Generalis**, in which there is an increase in curvature of the entire posterior corneal surface.
2. **Conscriptus**, in which there is a localized paracentral or central posterior corneal indentation (Fig. 5.144).

Sclerocornea

This is a rare, usually bilateral condition characterized by opacification and vascularization of the peripheral or entire cornea. If restricted to peripheral cornea the resulting 'scleralization' makes the cornea appear smaller (Fig. 5.145).

Keratectasia

This is a very rare, usually unilateral condition characterized by severe corneal opacification and protuberance between the eyelids. It is thought to be the result of intrauterine keratitis and perforation (Fig. 5.146).



Fig. 5.145
Sclerocornea (Courtesy of J. Salmon)



Fig. 5.146
Keratectasia

Contact lenses

Therapeutic uses

The risks of fitting a lens to an already compromised eye is greater than with lens wear for cosmetic reasons. The balance between benefit and risk should therefore be carefully considered. Close monitoring is vital to ensure early diagnosis and treatment of complications such as microbial keratitis. The choice of lens type is dictated by the nature of the ocular pathology.

Optical

To improve visual acuity when this cannot be achieved by spectacles in the following conditions:

1. **Irregular astigmatism** associated with keratoconus can be corrected with a rigid contact lens long after spectacles have failed and long before corneal grafting becomes necessary. Patients with astigmatism following corneal grafting may also benefit.
2. **Superficial corneal irregularities** can be neutralized by a rigid contact lens, which provides a smoother and optically more regular surface. Visual acuity can thus be improved, provided the irregularities are not too severe.
3. **Anisometropia** in which binocular vision cannot be achieved by spectacles (due to aniseikonia and prismatic effects) as may occur following cataract surgery.

Promotion of epithelial healing

1. **Persistent epithelial defects** often heal more quickly if the regenerating corneal epithelium is protected from the constant rubbing action of the lids. This allows the development of hemidesmosomal attachments to the basement membrane.
2. **Recurrent corneal erosions**, if associated with epithelial basement membrane dystrophy, may require long-term lens wear. In post-traumatic cases, lens wear can usually be discontinued after a few weeks. Lens wear may also provide comfort.

Pain relief

1. **Bullous keratopathy** can be managed with soft bandage contact lenses, which relieve pain by protecting the exposed corneal nerve endings from the shearing force of the eyelid during blinking. The lens may also flatten bullae into diffuse fine epithelial oedema. Instillation of hypertonic 5% saline may further osmotically reduce oedema and improve vision. The bullae gradually subside as corneal scarring supervenes and the patient can be weaned off lens wear.
2. **Wet filamentary keratitis** associated with profuse lacrimation, as seen in patients with brain stem strokes

and essential blepharospasm, can be treated with soft contact lenses and preservative-free acetylcysteine.
3. **Protection of corneal epithelium** from aberrant lashes.
4. **Thygeson superficial punctate keratitis**.

Preservation of corneal integrity

1. **A descemetocele** can be temporarily capped with a tight-fitting large-diameter soft or scleral lens to prevent perforation and allow natural healing to occur.
2. **Splinting** and apposition of the edges of a small corneal wound can be achieved by a contact lens which supports the cornea during healing. Examples include trauma, graft dehiscence, wound gape following cataract surgery, leaking trabeculectomy and accidental perforation during radial keratotomy. Slightly larger perforations may be sealed with glue (cyanoacrylate adhesive) followed by insertion of a bandage contact lens to protect the glue and prevent irritation of the lids from the glue's rough surface (Fig. 5.147).

Miscellaneous

1. **Ptosis props** to support the upper lids in patients with ocular myopathies.
2. **Maintenance of the fornices** to prevent symblepharon formation in eyes with cicatrizing conjunctivitis.
3. **Drug delivery** can be enhanced by a hydrogel lens imbibed with topical medication which increases exposure to the drug.

Complications

Allergic conjunctivitis

1. **Cause** is allergy to thiomersal, a preservative in contact lens care solutions, which was formerly a common problem with soft contact lenses. At one time, at least 10% of soft contact lens wearers were allergic to thiomersal. Fewer solutions now contain this ingredient.

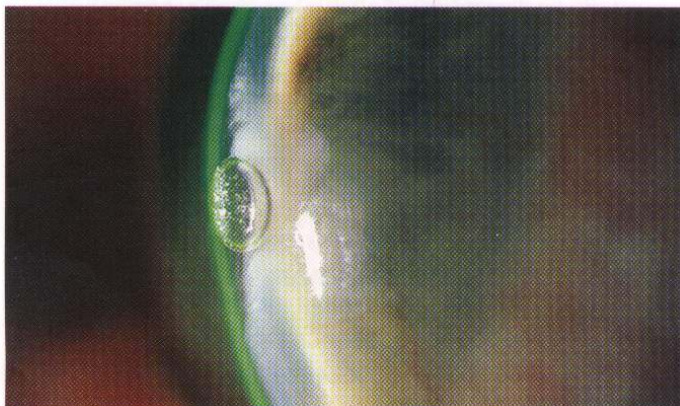


Fig. 5.147
Bandage contact lens following the application of glue to seal a corneal perforation

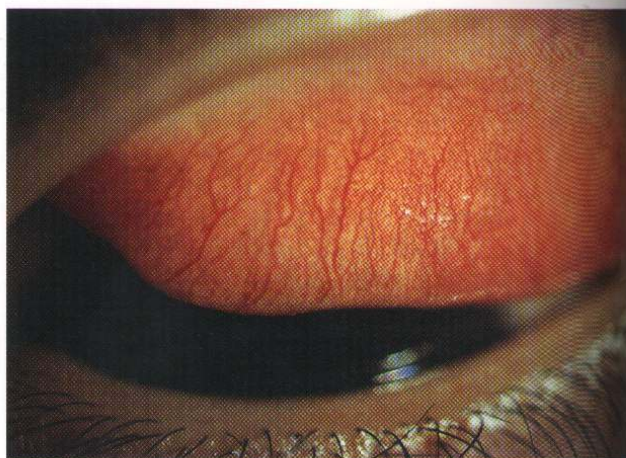


Fig. 5.148
Fine papillary reaction in contact lens-induced allergic conjunctivitis

2. **Presentation** is with redness, burning and itching soon after lens insertion. These symptoms may develop within days to months following initial exposure to thiomersal.
3. **Signs**
   - Perilimbal injection and a fine papillary conjunctival reaction (Fig. 5.148).
   - Grey epithelium extending from the superior limbus towards the axial cornea.
4. **Treatment** involves avoidance of thiomersal. The lenses should be disinfected with heat and non-preserved saline, or with a 3% hydrogen peroxide system.

Giant papillary conjunctivitis (GPC)

1. **Causes**
   - Irritation of the superior palpebral conjunctiva by the edge of a poorly fitting contact lens.
   - Allergy to lens material. Although any contact lens can cause GPC, soft lenses are most frequently implicated.
   - An immunological reaction to the contact lens deposits, especially proteins (Fig. 5.149).



Fig. 5.149
Contact lens deposits (Courtesy of C. Barry)

NB: GPC may also occur secondary to protruding corneal sutures (see Fig. 6.5) and poorly fitting ocular prostheses.

2. **Presentation** may be months or years after beginning lens wear, with ocular itching after lens removal, increased mucus production in the morning, photophobia and decreased lens tolerance. Blurred vision may also occur either from deposits on the lens or when the lens is pulled towards the upper fornix by the upper lid.
3. **Signs**
   - The spectrum of changes on the upper tarsal conjunctiva ranges from a mild papillary response to the full-blown picture of GPC characterized by giant papillae (>0.3 mm) (Fig. 5.150).
   - Excessive mucus in the eye and on the contact lens.
   - Trantas' dots, limbitis and peripheral corneal infiltration may be present.
   - Mechanical ptosis in severe cases.



Fig. 5.150
Contact lens-induced giant papillary conjunctivitis (Courtesy of C. Barry)

4. **Treatment**
   - Lens hygiene should be optimized and the patient reinstructed in the use of care solutions.
   - Lens fitting may require adjustment to decrease edge lift and regular replacement to minimize protein deposition.
   - Change in lens type from soft to gas-permeable may be beneficial because the latter are less likely to cause GPC.
   - Topical treatment with a mast cell stabilizer is often effective but long-term steroids should be avoided.

Corneal complications

1. **Epithelial oedema** due to hypoxia secondary to overwear is usually reversible.
2. **Corneal vascularization**, most often at the superior limbus, may develop in response to lens-induced hypoxia, especially with extended-wear lenses. New vessels are typically subepithelial, although deeper stromal vascularization may also occur.
3. **Sterile corneal infiltrates** are usually peripheral and may be epithelial, subepithelial or anterior stromal. Usually asymptomatic and detected during routine follow-up, they usually disappear once contact lens wear has been discontinued. Resumption of lens wear is usually possible after revision of lens care and improvement of lens fit. A short course of topical steroids may also speed up resolution. It is, however, extremely important to remember that a corneal infiltrate may be an early manifestation of microbial keratitis. Epithelial integrity is of diagnostic importance. If breached it implies infection, if intact the infiltrate is probably sterile. Pain, discharge and anterior uveitis are also signs of infection.
4. **Microbial keratitis** is the most serious complication.
5. **Corneal warping** resulting in severe and permanent astigmatism may occur in some eyes as a response to chronic hypoxia, for example, following prolonged wear of impermeable lenses.